OIPE JC10
APR 15 2005
PATENT & TRADEMARK OFFICE

Sequence Listing

<110> de Sauvage, Frederic
Carpenter, David A.

<120> Patched-2 Antibodies

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<141> 1999-04-14

<150> US 60/081,884
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BEST AVAILABLE COPY

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Ser Leu Gly Cys Gly Ile Gln Arg His Cys Gly Lys Val Leu Phe
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Leu Gly Leu Leu Ala Phe Gly Ala Leu Ala Leu Gly Leu Arg Met
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Ala Ile Ile Glu Thr Asn Leu Glu Gln Leu Trp Val Glu Val Gly
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Ser Arg Val Ser Gln Glu Leu His Tyr Thr Lys Glu Lys Leu Gly
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Glu Glu Ala Ala Tyr Thr Ser Gln Met Leu Ile Gln Thr Ala Arg
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Gly Lys Ser Trp Asp Leu Asn Lys Ile Cys Tyr Lys Ser Gly Val
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Pro Leu Ile Glu Asn Gly Met Ile Glu Trp Met Ile Glu Lys Leu
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Phe Pro Cys Val Ile Leu Thr Pro Leu Asp Cys Phe Trp Glu Gly
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Ala Lys Leu Gln Gly Gly Ser Ala Tyr Leu Pro Gly Arg Pro Asp
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Ile Gln Trp Thr Asn Leu Asp Pro Glu Gln Leu Leu Glu Glu Leu
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Gly Pro Phe Ala Ser Leu Glu Gly Phe Arg Glu Leu Leu Asp Lys
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Ala Gln Val Gly Gln Ala Tyr Val Gly Arg Pro Cys Leu His Pro
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Asp Asp Leu His Cys Pro Pro Ser Ala Pro Asn His His Ser Arg
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Phe Ser His Lys Phe Met His Trp Gln Glu Glu Leu Leu Leu Gly
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Gly Met Ala Arg Asp Pro Gln Gly Glu Leu Leu Arg Ala Glu Ala
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Leu Gln Ser Thr Phe Leu Leu Met Ser Pro Arg Gln Leu Tyr Glu
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His Phe Arg Gly Asp Tyr Gln Thr His Asp Ile Gly Trp Ser Glu
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Glu Gln Ala Ser Thr Val Leu Gln Ala Trp Gln Arg Arg Phe Val
350 355 360

Gln Leu Ala Gln Glu Ala Leu Pro Glu Asn Ala Ser Gln Gln Ile
365 370 375

His Ala Phe Ser Ser Thr Thr Leu Asp Asp Ile Leu His Ala Phe
380 385 390

Ser Glu Val Ser Ala Ala Arg Val Val Gly Gly Tyr Leu Leu Met
395 400 405

Leu Ala Tyr Ala Cys Val Thr Met Leu Arg Trp Asp Cys Ala Gln
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Arg Arg His Cys Gln Arg Leu Asp Val Leu Cys Cys Phe Ser Ser
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Pro Cys Ser Ala Gln Val Ile Gln Ile Leu Pro Gln Glu Leu Gly
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Asp Gly Thr Val Pro Val Gly Ile Ala His Leu Thr Ala Thr Val
590 595 600

Gln Ala Phe Thr His Cys Glu Ala Ser Ser Gln His Val Val Thr
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Ile Leu Pro Pro Gln Ala His Leu Val Pro Pro Pro Ser Asp Pro
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Leu Pro Cys Ala Arg Trp Asn Leu Ala His Phe Ala Arg Tyr Gln
665 670 675

Phe Ala Pro Leu Leu Leu Gln Ser His Ala Lys Ala Ile Val Leu
680 685 690

Val Leu Phe Gly Ala Leu Leu Gly Leu Ser Leu Tyr Gly Ala Thr
695 700 705

Leu Val Gln Asp Gly Leu Ala Leu Thr Asp Val Val Pro Arg Gly
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Thr Lys Glu His Ala Phe Leu Ser Ala Gln Leu Arg Tyr Phe Ser
725 730 735

Leu Tyr Glu Val Ala Leu Val Thr Gln Gly Gly Phe Asp Tyr Ala
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His Ser Gln Arg Ala Leu Phe Asp Leu His Gln Arg Phe Ser Ser
755 760 765

Leu Lys Ala Val Leu Pro Pro Pro Ala Thr Gln Ala Pro Arg Thr
770 775 780

Trp Leu His Tyr Tyr Arg Asn Trp Leu Gln Gly Ile Gln Ala Ala
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Phe Asp Gln Asp Trp Ala Ser Gly Arg Ile Thr Arg His Ser Tyr
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Arg Asn Gly Ser Glu Asp Gly Ala Leu Ala Tyr Lys Leu Leu Ile
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Gln Thr Gly Asp Ala Gln Glu Pro Leu Asp Phe Ser Gln Leu Thr
830 835 840

Thr Arg Lys Leu Val Asp Arg Glu Gly Leu Ile Pro Pro Glu Leu
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Phe Tyr Met Gly Leu Thr Val Trp Val Ser Ser Asp Pro Leu Gly
860 865 870

Leu Ala Ala Ser Gln Ala Asn Phe Tyr Pro Pro Pro Pro Glu Trp

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Leu His Asp Lys Tyr Asp Thr Thr Gly Glu Asn Leu Arg Ile Pro
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Gly Leu Gln Lys Thr Ala Asp Phe Val Glu Ala Ile Glu Gly Ala
920 925 930

Arg Ala Ala Cys Ala Glu Ala Gly Gln Ala Gly Val His Ala Tyr
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Pro Ser Gly Ser Pro Phe Leu Phe Trp Glu Gln Tyr Leu Gly Leu
950 955 960

Arg Arg Cys Phe Leu Leu Ala Val Cys Ile Leu Leu Val Cys Thr
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Phe Leu Val Cys Ala Leu Leu Leu Leu Asn Pro Trp Thr Ala Gly
980 985 990

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Phe Asp Phe Ile Val Arg Tyr Phe Phe Ala Ala Leu Thr Val Leu
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Thr Leu Leu Gly Leu Leu His Gly Leu Val Leu Leu Pro Val Leu
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Glu Ser Pro Glu Ile Leu Ser Pro Pro Ala Pro Gln Gly Gly Gly
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Leu Arg Trp Gly Ala Ser Ser Ser Leu Pro Gln Ser Phe Ala Arg
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Pro	Leu	Trp	Leu	Arg	Ala	Lys	Phe	Gln	Arg	Leu	Leu	Phe	Lys	Leu
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His	Leu	Cys	Tyr	Lys	Ser	Gly	Glu	Leu	Ile	Thr	Glu	Thr	Gly	Tyr
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Pro	Leu	Asp	Cys	Phe	Trp	Glu	Gly	Ala	Lys	Leu	Gln	Ser	Gly	Thr
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Tyr Met Asp Arg Pro Cys Leu Asn Pro Ala Asp Pro Asp Cys Pro
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Arg Val Ala Ser Gly Tyr Leu Leu Met Leu Ala Tyr Ala Cys Leu
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Thr Met Leu Arg Trp Asp Cys Ser Lys Ser Gln Gly Ala Val Gly
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Pro Arg Ser Glu Ile Ser Val Gln Pro Val Thr Val Thr Gln Asp
635 640 645

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Pro Cys Thr Lys Trp Thr Leu Ser Ser Phe Ala Glu Lys His Tyr
680 685 690

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Arg Glu Tyr Asp Phe Ile Ala Ala Gln Phe Lys Tyr Phe Ser Phe
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755 760 765

Gln His Leu Leu Tyr Asp Leu His Arg Ser Phe Ser Asn Val Lys
770 775 780

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785 790 795

His Tyr Phe Arg Asp Trp Leu Gln Gly Leu Gln Asp Ala Phe Asp
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Ser Asp Trp Glu Thr Gly Lys Ile Met Pro Asn Asn Tyr Lys Asn
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Gly Ser Asp Asp Gly Val Leu Ala Tyr Lys Leu Leu Val Gln Thr
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845 850 855

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Ile Tyr Leu Thr Ala Trp Val Ser Asn Asp Pro Val Ala Tyr Ala
875 880 885

Ala Ser Gln Ala Asn Ile Arg Pro His Arg Pro Glu Trp Val His
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935 940 945

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950 955 960

Asn Gly Tyr Pro Phe Leu Phe Trp Glu Gln Tyr Ile Gly Leu Arg
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His Trp Leu Leu Leu Phe Ile Ser Val Val Leu Ala Cys Thr Phe
980 985 990

Leu Val Cys Ala Val Phe Leu Leu Asn Pro Trp Thr Ala Gly Ile
995 1000 1005

Ile Val Met Val Leu Ala Leu Met Thr Val Glu Leu Phe Gly Met
1010 1015 1020

Met Gly Leu Ile Gly Ile Lys Leu Ser Ala Val Pro Val Val Ile
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Val Ser Thr Leu Leu Gly Val Leu Met Leu Ala Gly Ser Glu Phe
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Asp Phe Ile Val Arg Tyr Phe Phe Ala Val Leu Ala Ile Leu Thr
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Ile Leu Gly Val Leu Asn Gly Leu Val Leu Leu Pro Val Leu Leu

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Ser Phe Phe Gly Pro Tyr Pro Glu Val Ser Pro Ala Asn Gly Leu
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1145 1150 1155

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1160 1165 1170

Ser Asp Ser Glu Tyr Ser Ser Gln Thr Thr Val Ser Gly Leu Ser
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Glu Glu Leu Arg His Tyr Glu Ala Gln Gln Gly Ala Gly Gly Pro
1190 1195 1200

Ala His Gln Val Ile Val Glu Ala Thr Glu Asn Pro Val Phe Ala
1205 1210 1215

His Ser Thr Val Val His Pro Glu Ser Arg His His Pro Pro Ser
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Gly Arg Gln Gly Gln Gln Pro Arg Arg Asp Pro Pro Arg Glu Gly
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Leu Trp Pro Pro Leu Tyr Arg Pro Arg Arg Asp Ala Phe Glu Ile
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Ser Thr Glu Gly His Ser Gly Pro Ser Asn Arg Ala Arg Trp Gly
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Pro Arg Gly Ala Arg Ser His Asn Pro Arg Asn Pro Ala Ser Thr
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Ala Met Gly Ser Ser Val Pro Gly Tyr Cys Gln Pro Ile Thr Thr
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Val Thr Ala Ser Ala Ser Val Thr Val Ala Val His Pro Pro Pro
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Val Pro Gly Pro Gly Arg Asn Pro Arg Gly Gly Leu Cys Pro Gly
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Tyr Pro Glu Thr Asp His Gly Leu Phe Glu Asp Pro His Val Pro
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Phe His Val Arg Cys Glu Arg Arg Asp Ser Lys Val Glu Val Ile
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Ser Leu Gly Cys Arg Ile Gln Lys His Cys Gly Lys Val Leu Phe
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Leu Gly Leu Val Ala Phe Gly Ala Leu Ala Leu Gly Leu Arg Val
65                  70                  75

Ala Val Ile Glu Thr Asp Leu Glu Gln Leu Trp Val Glu Val Gly
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Ser Arg Val Ser Gln Glu Leu His Tyr Thr Lys Glu Lys Leu Gly
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Glu Glu Ala Ala Tyr Thr Ser Gln Met Leu Ile Gln Thr Ala His
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Gln Glu Gly Gly Asn Val Leu Thr Pro Glu Ala Leu Asp Leu His
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Leu Gln Ala Ala Leu Thr Ala Ser Lys Val Gln Val Ser Leu Tyr
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Gly Lys Ser Trp Asp Leu Asn Lys Ile Cys Tyr Lys Ser Gly Val
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Pro Leu Ile Glu Asn Gly Met Ile Glu Arg Met Ile Glu Lys Leu
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Phe Pro Cys Val Ile Leu Thr Pro Leu Asp Cys Phe Trp Glu Gly
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Ala Lys Leu Gln Gly Gly Ser Ala Tyr Leu Pro Gly Arg Pro Asp
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Ile Gln Trp Thr Asn Leu Asp Pro Gln Gln Leu Leu Glu Glu Leu
            215                 220                 225

Gly Pro Phe Ala Ser Leu Glu Gly Phe Arg Glu Leu Leu Asp Lys
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Ala Gln Val Gly Gln Ala Tyr Val Gly Arg Pro Cys Leu Asp Pro
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Asp Asp Pro His Cys Pro Pro Ser Ala Pro Asn Arg His Ser Arg
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Gln Ala Pro Asn Val Ala Gln Glu Leu Ser Gly Gly Cys His Gly
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Phe Ser His Lys Phe Met His Trp Gln Glu Glu Leu Leu Leu Gly
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Gly Thr Ala Arg Asp Leu Gln Gly Gln Leu Leu Arg Ala Glu Ala
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His Phe Arg Gly Asp Tyr Gln Thr His Asp Ile Gly Trp Ser Glu
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Glu Gln Ala Ser Met Val Leu Gln Ala Trp Gln Arg Arg Phe Val
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Gln Leu Ala Gln Glu Ala Leu Pro Ala Asn Ala Ser Gln Gln Ile
365 370 375

His Ala Phe Ser Ser Thr Thr Leu Asp Asp Ile Leu Arg Ala Phe
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Ser Glu Val Ser Thr Thr Arg Val Val Gly Gly Tyr Leu Leu Met
395 400 405

Leu Ala Tyr Ala Cys Val Thr Met Leu Arg Trp Asp Cys Ala Gln
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Ser Gln Gly Ala Val Gly Leu Ala Gly Val Leu Leu Val Ala Leu
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Ala Val Ala Ser Gly Leu Gly Leu Cys Ala Leu Leu Gly Ile Thr
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Phe Asn Ala Ala Thr Thr Gln Val Leu Pro Phe Leu Ala Leu Gly
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Ile Gly Val Asp Asp Ile Phe Leu Leu Ala His Ala Phe Thr Lys
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Ala Pro Pro Asp Thr Pro Leu Pro Glu Arg Met Gly Glu Cys Leu
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Arg Ser Thr Gly Thr Ser Val Ala Leu Thr Ser Val Asn Asn Met
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Val Ala Phe Phe Met Ala Ala Leu Val Pro Ile Pro Ala Leu Arg
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Ala Val Met Leu Val Phe Pro Ala Ile Leu Ser Leu Asp Leu Arg
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Arg Arg His Arg Gln Arg Leu Asp Val Leu Cys Cys Phe Ser Ser
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Pro Cys Ser Ala Gln Val Ile Gln Met Leu Pro Gln Glu Leu Gly
575 580 585

Asp Arg Ala Val Pro Val Gly Ile Ala His Leu Thr Ala Thr Val

590 595 600

Gln Ala Phe Thr His Cys Glu Ala Ser Ser Gln His Val Val Thr
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Ile Leu Pro Pro Gln Ala His Leu Leu Ser Pro Ala Ser Asp Pro
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Leu Leu Cys Ala His Trp Thr Leu Ala His Phe Ala Arg Tyr Gln
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Phe Ala Pro Leu Leu Leu Gln Thr Arg Ala Lys Ala Leu Val Leu
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695 700 705

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725 730 735

Leu Tyr Glu Val Ala Leu Val Thr Gln Gly Gly Phe Asp Tyr Ala
740 745 750

His Ser Gln Arg Ala Leu Phe Asp Leu His Gln Arg Phe Ser Ser
755 760 765

Leu Lys Ala Val Leu Pro Pro Pro Ala Thr Gln Ala Pro Arg Thr
770 775 780

Trp Leu His Tyr Tyr Arg Ser Trp Leu Gln Gly Ile Gln Ala Ala
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Phe Asp Gln Asp Trp Ala Ser Gly Arg Ile Thr Cys His Ser Tyr
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Arg Asn Gly Ser Glu Asp Gly Ala Leu Ala Tyr Lys Leu Leu Ile
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Gln Thr Gly Asn Ala Gln Glu Pro Leu Asp Phe Ser Gln Leu Thr
830 835 840

Thr Arg Lys Leu Val Asp Lys Glu Gly Leu Ile Pro Pro Glu Leu
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Phe Tyr Met Gly Leu Thr Val Trp Val Ser Ser Asp Pro Leu Gly
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875 880 885

Leu His Asp Lys Tyr Asp Thr Thr Gly Glu Asn Leu Arg Ile Pro
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Gly Leu Gln Lys Thr Ala Asp Phe Val Glu Ala Ile Glu Gly Ala
920 925 930

Arg Ala Ala Cys Thr Glu Ala Gly Gln Ala Gly Val His Ala Tyr
935 940 945

Pro Ser Gly Ser Pro Phe Leu Phe Trp Glu Gln Tyr Leu Gly Leu
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980 985 990

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995 1000 1005

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Ile Leu Val Ala Ser Ile Gly Ile Gly Val Glu Phe Thr Val His
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Val Ala Leu Gly Phe Leu Thr Ser His Gly Ser Arg Asn Leu Arg
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Phe Asp Phe Ile Ile Arg Tyr Phe Phe Val Val Leu Thr Val Leu
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Thr Leu Leu Gly Leu Leu His Gly Leu Leu Leu Leu Pro Val Leu
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501 GCAGCCGGGT GAGCCAGGAG CTGCATTACA CCAAGGAGAA GCTGGGGGAG GAGGCTGCAT ACACCTCTCA GATGCTGATA CAGACCGCAC GCCAGGAGGG
    CGTCGGCCCA CTCGGTCCTC GACGTAATGT GGTTCCTCTT CGACCCCCTC CTCCGACGTA TGTGGAGAGT CTACGACTAT GTCTGGCGTG CGGTCCTCCC
 91   S  R  V  S  Q  E  L  H  Y  T  K  E  K  L  G  E  E  A  A  Y  T  S  Q  M  L  I  Q  T  A  R  Q  E  G

601 AGAGAACATC CTCACACCCG AAGCACTTGG CCTCCACCTC CAGGCAGCCC TCACTGCCAG TAAAGTCCAA GTATCACTCT ATGGGAAGTC CTGGGATTTG
    TCTCTTGTAG GAGTGTGGGC TTCGTGAACC GGAGGTGGAG GTCCGTCGGG AGTGACGGTC ATTTCAGGTT CATAGTGAGA TACCCTTCAG GACCCTAAAC
124 E  N  I  L  T  P  E  A  L  G  L  H  L  Q  A  A  L  T  A  S  K  V  Q  V  S  L  Y  G  K  S  W  D  L

701 AACAAAATCT GCTACAAGTC AGGAGTTCCC CTTATTGAAA ATGGAATGAT TGAGTGGATG ATTGAGAAGC TGTTTCCGTG CGTGATCCTC ACCCCCCTCG
    TTGTTTTAGA CGATGTTCAG TCCTCAAGGG GAATAACTTT TACCTTACTA ACTCACCTAC TAACTCTTCG ACAAAGGCAC GCACTAGGAG TGGGGGGAGC
157 N  K  I  C  Y  K  S  G  V  P  L  I  E  N  G  M  I  E  W  M  I  E  K  L  F  P  C  V  I  L  T  P  L  D
```

FIG._1A

Docket No.: P1405R1C1

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801 ACTGCTTCTG GGAGGGAGCC AAACTCCAAG GGGGCTCCGC CTACCTGCCC GGCCGCCCGG ATATCCAGTG GACCAACCTG GATCCAGAGC AGCTGCTGGA
    TGACGAAGAC CCTCCCTCGG TTTGAGGTTC CCCCGAGGCG GATGGACGGG CCGGCGGGCC TATAGGTCAC CTGGTTGGAC CTAGGTCTCG TCGACGACCT
191   C  F  W  E  G  A  K  L  Q  G  G  S  A  Y  L  P  G  R  P  D  I  Q  W  T  N  L  D  P  E  Q  L  L  E

901 GGAGCTGGGT CCCTTTGCCT CCCTTGAGGG CTTCCGGGAG CTGCTAGACA AGGCACAGGT GGGCCAGGCC TACGTGGGGC GGCCCTGTCT GCACCCTGAT
    CCTCGACCCA GGGAAACGGA GGGAACTCCC GAAGGCCCTC GACGATCTGT TCCGTGTCCA CCCGGTCCGG ATGCACCCCG CCGGGACAGA CGTGGGACTA
224 E  L  G  P  F  A  S  L  E  G  F  R  E  L  L  D  K  A  Q  V  G  Q  A  Y  V  G  R  P  C  L  H  P  D

1001 GACCTCCACT GCCCACCTAG TGCCCCCAAC CATCACAGCA GGCAGGCTCC CAATGTGGCT CACGAGCTGA GTGGGGGCTG CCATGGCTTC TCCCACAAAT
     CTGGAGGTGA CGGGTGGATC ACGGGGGTTG GTAGTGTCGT CCGTCCGAGG GTTACACCGA GTGCTCGACT CACCCCCGAC GGTACCGAAG AGGGTGTTTA
257 D  L  H  C  P  P  S  A  P  N  H  H  S  R  Q  A  P  N  V  A  H  E  L  S  G  G  C  H  G  F  S  H  K  F

1101 TCATGCACTG GCAGGAGGAA TTGCTGCTGG GAGGCATGGC CAGAGACCCC CAAGGAGAGC TGCTGAGGGC AGAGGCCCTG CAGAGCACCT TCTTGCTGAT
     AGTACGTGAC CGTCCTCCTT AACGACGACC CTCCGTACCG GTCTCTGGGG GTTCCTCTCG ACGACTCCCG TCTCCGGGAC GTCTCGTGGA AGAACGACTA
291   M  H  W  Q  E  E  L  L  L  G  G  M  A  R  D  P  Q  G  E  L  L  R  A  E  A  L  Q  S  T  F  L  L  M

1201 GAGTCCCCGC CAGCTGTACG AGCATTTCCG GGGTGACTAT CAGACACATG ACATTGGCTG GAGTGAGGAG CAGGCCAGCA CAGTGCTACA AGCCTGGCAG
     CTCAGGGGCG GTCGACATGC TCGTAAAGGC CCCACTGATA GTCTGTGTAC TGTAACCGAC CTCACTCCTC GTCCGGTCGT GTCACGATGT TCGGACCGTC
324 S  P  R  Q  L  Y  E  H  F  R  G  D  Y  Q  T  H  D  I  G  W  S  E  E  Q  A  S  T  V  L  Q  A  W  Q

1301 CGGCGCTTTG TGCAGCTGGC CCAGGAGGCC CTGCCTGAGA ACGCTTCCCA GCAGATCCAT GCCTTCTCCT CCACCACCCT GGATGACATC CTGCATGCGT
     GCCGCGAAAC ACGTCGACCG GGTCCTCCGG GACGGACTCT TGCGAAGGGT CGTCTAGGTA CGGAAGAGGA GGTGGTGGGA CCTACTGTAG GACGTACGCA
357 R  R  F  V  Q  L  A  Q  E  A  L  P  E  N  A  S  Q  Q  I  H  A  F  S  S  T  T  L  D  D  I  L  H  A  F

1401 TCTCTGAAGT CAGTGCTGCC CGTGTGGTGG GAGGCTATCT GCTCATGCTG GCCTATGCCT GTGTGACCAT GCTGCGGTGG GACTGCGCCC AGTCCCAGGG
     AGAGACTTCA GTCACGACGG GCACACCACC CTCCGATAGA CGAGTACGAC CGGATACGGA CACACTGGTA CGACGCCACC CTGACGCGGG TCAGGGTCCC
391   S  E  V  S  A  A  R  V  V  G  G  Y  L  L  M  L  A  Y  A  C  V  T  M  L  R  W  D  C  A  Q  S  Q  G

1501 TTCCGTGGGC CTTGCCGGGG TACTGCTGGT GGCCCTGGCG GTGGCCTCAG GCCTTGGGCT CTGTGCCCTG CTCGGCATCA CCTTCAATGC TGCCACTACC
     AAGGCACCCG GAACGGCCCC ATGACGACCA CCGGGACCGC CACCGGAGTC CGGAACCCGA GACACGGGAC GAGCCGTAGT GGAAGTTACG ACGGTGATGG
424 S  V  G  L  A  G  V  L  L  V  A  L  A  V  A  S  G  L  G  L  C  A  L  L  G  I  T  F  N  A  A  T  T
```

FIG._1B

```
                30        40        50        60        70
905531      GCTGGGGTGCACGCCTACCNCAGCGGNTCCCCCTTCCTCTTCTGGGAACA
              ::: ::  :   ******* ***** ******************** **
hpatched    CTGGGGCTGTCCAGTTACCCCAACGGCTACCCCTTCCTCTTCTGGGAGCA
          3010      3020      3030      3040      3050

                80        90        100       110       120
905531      GTATCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGG
            ***  * ***** ** * ***  * ******  * ** ** *  ** ***
hpatched    GTACATCGGCCTCCGCCACTGGCTGCTGCTGTTCATCAGCGTGGTGTTGG
          3060      3070      3080      3090      3100

                130       140       150       160       170
905531      TGTGCACTTTCCTCGTCTGTGCTCTGCTGCTCCTNAACCCCTGGACGGCT
              ***** ******** ** *** *  * ** ******************
hpatched    CCTGCACATTCCTCGTGTGCGCTGTCTTCCTTCTGAACCCCTGGACGGCC
          3110      3120      3130      3140      3150

                180       190       200       210       220
905531      GGCCTNATAGTGCTGGTCCTGGCGATGATGACAGTGGAACTCTTTGGTAT
            **  **** *** ********** ******* ** ** ** ** ** **
hpatched    GGGATCATTGTGATGGTCCTGGCGCTGATGACGGTCGAGCTGTTCGGCAT
          3160      3170      3180      3190      3200

                230       240       250
905531      CATGGGTTTNCTGGGCATCAAGCTGAGT
             *****  ** * ** ******** ***
hpatched    GATGGGCCTCATCGGAATCAAGCTCAGT
          3210      3220      3230
```

```
                80        90        100       110       120
905531      TCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGGTGT
             :::   :::     * ** *  ** *****   ****   * ** ****
hpatched    GCTGCTGCTGTTCATCAGCGTGGTGTTGGCC---TGCACATTCCTCGTGT
                  3090      3100      3110      3120

                130       140       150
905531      GCACTTTCCTCGTCTGTGCTCTGCTGCT
            ** ** ** ** *       :   :
hpatched    GCGCTGTCTTCCTTCTGAACCCCTGGAC
          3130      3140      3150
```

FIG._2A

```
                30        40        50        60        70
1326258     GCTGGGGTGCACGCCTACCCCAGCGGCTCCCCCTTCCTCTTCTGGGAACA
               ::: ::   :   ******* ***** ****************** **
hpatched    CTGGGGCTGTCCAGTTACCCCAACGGCTACCCCTTCCTCTTCTGGGAGCA
          3010      3020      3030      3040      3050

                80        90       100       110       120
1326258     GTATCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGG
            ***  * ***** ** * ***  * ******  * ** ** *  ** ***
hpatched    GTACATCGGCCTCCGCCACTGGCTGCTGCTGTTCATCAGCGTGGTGTTGG
          3060      3070      3080      3090      3100

              130       140       150
1326258     TGTGCACTTTCCTCNTCTGTGCTCT
             ***** ******** ** *** *
hpatched    CCTGCACATTCCTCGTGTGCGCTGT
          3110      3120      3130
```

```
                 90       100       110       120       130
1326258     TCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGGTGT
             :::   :::     * ** *  ** *****   ****   * ** ****
hpatched    GCTGCTGCTGTTCATCAGCGTGGTGTTGGCC---TGCACATTCCTCGTGT
                3090      3100      3110          3120

               140       150
1326258     GCACTTTCCTCNTCTGTGCTCT
            ** ** ** ****       :
hpatched    GCGCTGTCTTCCTTCTGAACCC
          3130      3140
```

```
                10        20        30        40        50
1326258       CCGGGCAGCATGCGCAGAGGCCGGCCAGGCTGGGGTGCACGCCTACCCCA
              ****** *****    ** ** * *** ******* *      :
hpatched.RC   CCGGGCGGCATG--GCGAAGCGGACCACGCTGGGGGGTGGCTCAGGGGAG
            710       720       730       740       750
```

FIG._2B

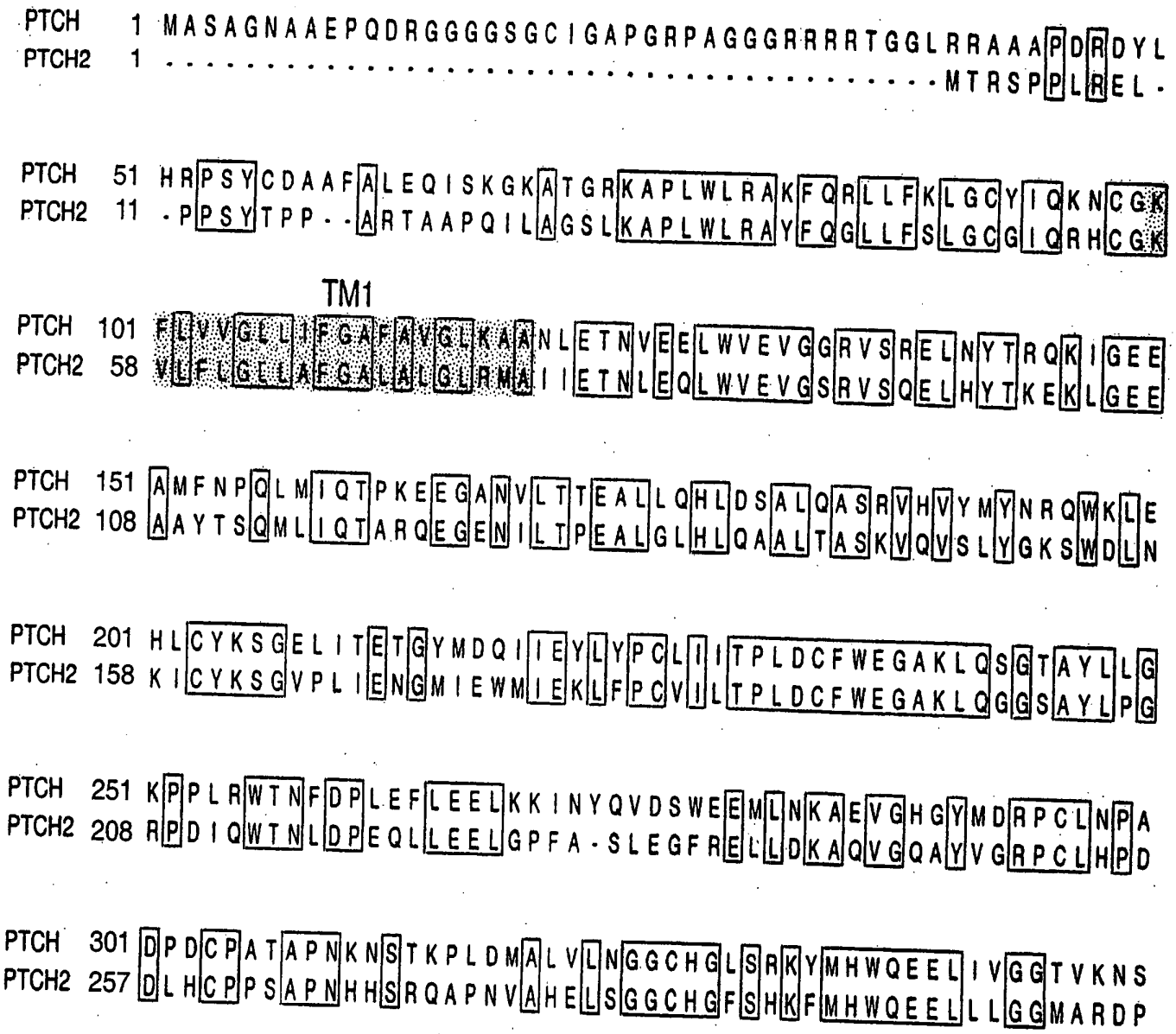
PTCH 1 MASAGNAAEPQDRGGGGSGCIGAPGRPAGGGRRRRTGGLRRAAAPDRDYL
PTCH2 1 ----------MTRSPPLRELR
PTCH 51 HRPSYCDAAFALEQISKGKATGRKAPLWLRAKFQRLLFKLGCYIQKNCGK
PTCH2 11 PPSYTPP--ARTAAPQILAGSLKAPLWLRAYFQGLLFSLGCGIQRHCGK
TM1
PTCH 101 FLVVGLLIFGAFAVGLKAANLETNVEELWVEVGGRVSRELNYTRQKIGEE
PTCH2 58 VLFLGLLAFGALALGLRMAIIETNLEQLWVEVGSRVSQELHYTKEKLGEE
PTCH 151 AMFNPQLMIQTPKEEGANVLTTEALLQHLDSALQASRVHVYMYNRQWKLE
PTCH2 108 AAYTSQMLIQTARQEGENILTPEALGLHLQAALTASKVQVSLYGKSWDLN
PTCH 201 HLCYKSGELITETGYMDQIIEYLYPCLIITPLDCFWEGAKLQSGTAYLLG
PTCH2 158 KICYKSGVPLIENGMIEWMIEKLFPCVILTPLDCFWEGAKLQGGSAYLPG
PTCH 251 KPPLRWTNFDPLEFLEELKKINYQVDSWEEMLNKAEVGHGYMDRPCLNPA
PTCH2 208 RPDIQWTNLDPEQLLEELGPFA-SLEGFRELLDKAQVGQAYVGRPCLHPD
PTCH 301 DPDCPATAPNKNSTKPLDMALVLNGGCHGLSRKYMHWQEELIVGGTVKNS
PTCH2 257 DLHCPPSAPNHHSRQAPNVAHELSGGCHGFSHKFMHWQEELLLGGMARDP

FIG._3A

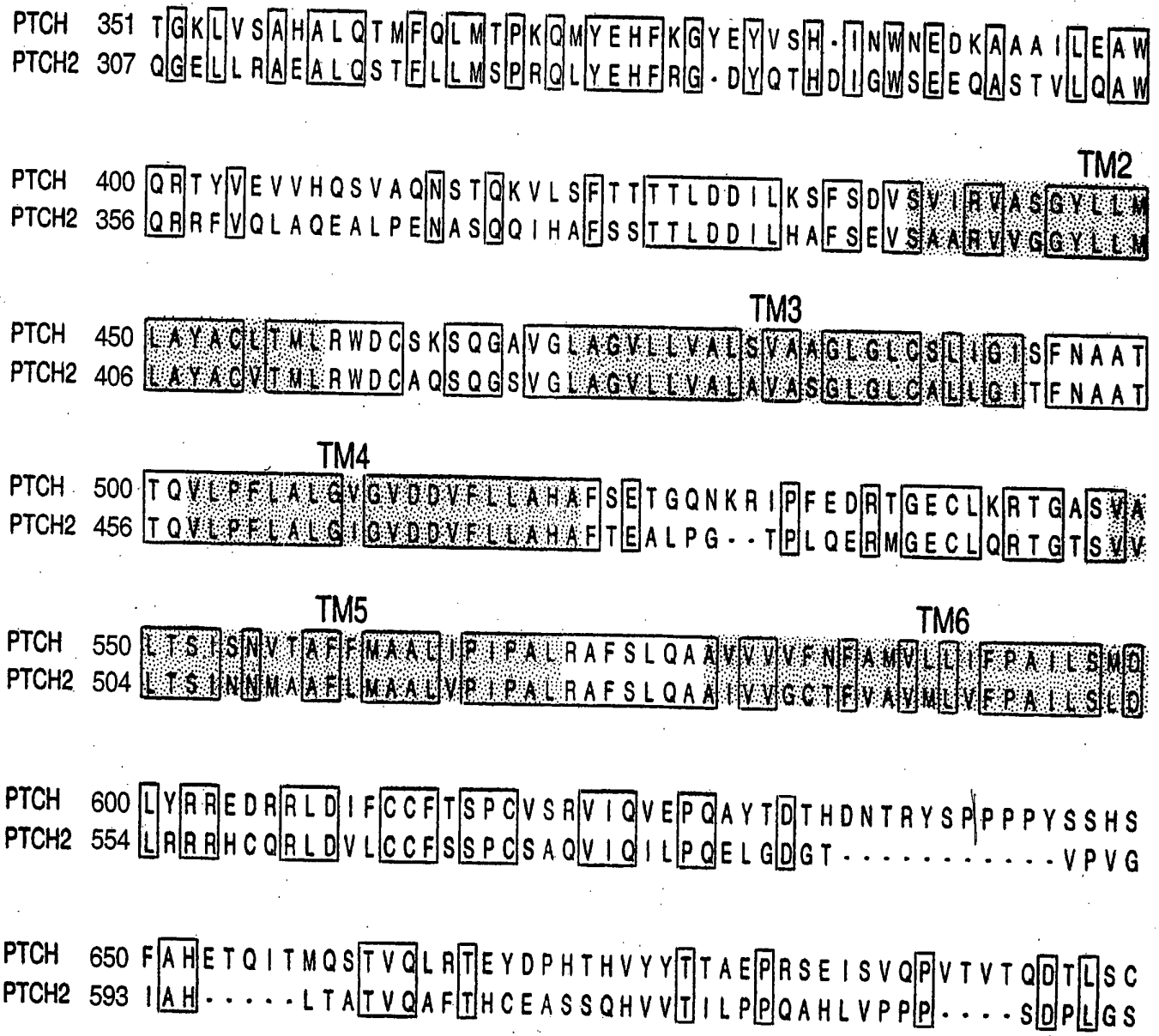
PTCH 351 TGKLVSAHALQTMFQLMTPKQMYEHFKGYEYVSH-INWNEDKAAAILEAW
PTCH2 307 QGELLRAEALQSTFLLMSPRQLYEHFRG-DYQTHDIGWSEEQASTVLQAW
TM2
PTCH 400 QRTYVEVVHQSVAQNSTQKVLSFTTTTLDDILKSFSDVSVIRVASGYLLM
PTCH2 356 QRRFVQLAQEALPENASQQIHAFSSTTLDDILHAFSEVSAARVVGGYLLM
TM3
PTCH 450 LAYACLTMLRWDCSKSQGAVGLAGVLLVALSVAAGLGLCSLIGISFNAAT
PTCH2 406 LAYACVTMLRWDCAQSQGSVGLAGVLLVALAVASGLGLCALLGITFNAAT
TM4
PTCH 500 TQVLPFLALGVGVDDVFLLAHAFSETGQNKRIPFEDRTGECLKRTGASVA
PTCH2 456 TQVLPFLALGIGVDDVFLLAHAFTEALPG--TPLQERMGECLQRTGTSVV
TM5
TM6
PTCH 550 LTSISNVTAFFMAALIPIPALRAFSLQAAVVVVFNFAMVLLIFPAILSMD
PTCH2 504 LTSINNMAAFLMAALVPIPALRAFSLQAAIVVGCTFVAVMLVFPAILSLD
PTCH 600 LYRREDRRLDIFCCFTSPCVSRVIQVEPQAYTDTHDNTRYSPPPPYSSHS
PTCH2 554 LRRRHCQRLDVLCCFSSPCSAQVIQILPQELGDGT----------VPVG
PTCH 650 FAHETQITMQSTVQLRTEYDPHTHVYYTTAEPRSEISVQPVTVTQDTLSC
PTCH2 593 IAH-----LTATVQAFTHCEASSQHVVTILPPQAHLVPPP----SDPLGS

FIG._3B

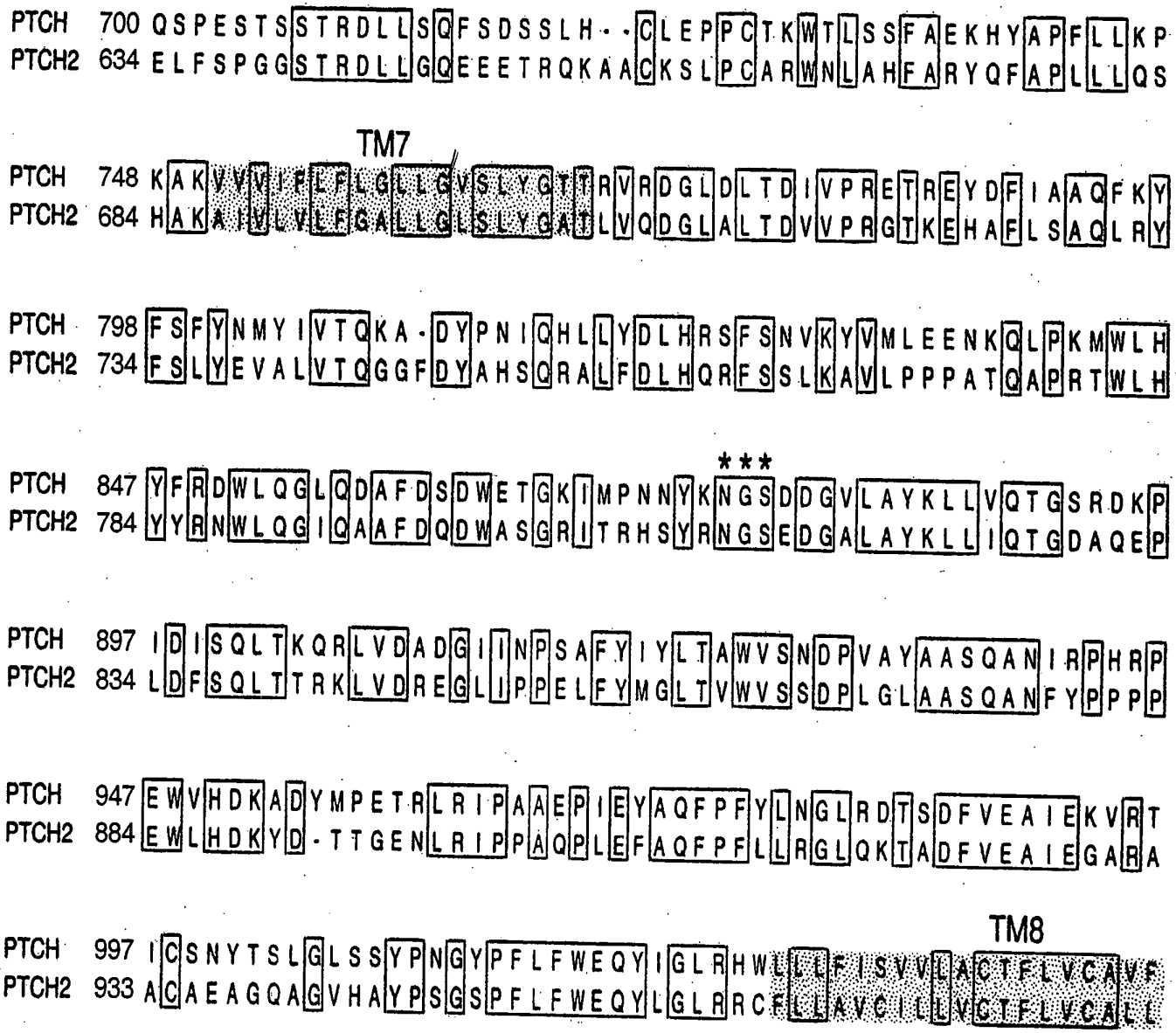
PTCH 700 QSPESTSSTRDLLSQFSDSSLH--CLEPPCTKWTLSSFAEKHYAPFLLKP
PTCH2 634 ELFSPGGSTRDLLGQEEETRQKAACKSLPCARWNLAHFARYQFAPLLLQS
TM7
PTCH 748 KAKVVVIFLFLGLLGVSLYGTTRVRDGLDLTDIVPRETREYDFIAAQFKY
PTCH2 684 HAKAIVLVLFGALLGLSLYGATLVQDGLALTDVVPRGTKEHAFLSAQLRY
PTCH 798 FSFYNMYIVTQKA-DYPNIQHLLYDLHRSFSNVKYVMLEENKQLPKMWLH
PTCH2 734 FSLYEVALVTQGGFDYAHSQRALFDLHQRFSSLKAVLPPPATQAPRTWLH
***
PTCH 847 YFRDWLQGLQDAFDSDWETGKIMPNNYKNGSDDGVLAYKLLVQTGSRDKP
PTCH2 784 YYRNWLQGIQAAFDQDWASGRITRHSYRNGSEDGALAYKLLIQTGDAQEP
PTCH 897 IDISQLTKQRLVDADGIINPSAFYIYLTAWVSNDPVAYAASQANIRPHRP
PTCH2 834 LDFSQLTTRKLVDREGLIPPELFYMGLTVWVSSDPLGLAASQANFYPPPP
PTCH 947 EWVHDKADYMPETRLRIPAAEPIEYAQFPFYLNGLRDTSDFVEAIEKVRT
PTCH2 884 EWLHDKYD-TTGENLRIPPAQPLEFAQFPFLLRGLQKTADFVEAIEGARA
TM8
PTCH 997 ICSNYTSLGLSSYPNGYPFLFWEQYIGLRHWLLLFISVVLACTFLVCAVF
PTCH2 933 ACAEAGQAGVHAYPSGSPFLFWEQYLGLRRCFLLAVCILLVCTFLVCALL

FIG._3C

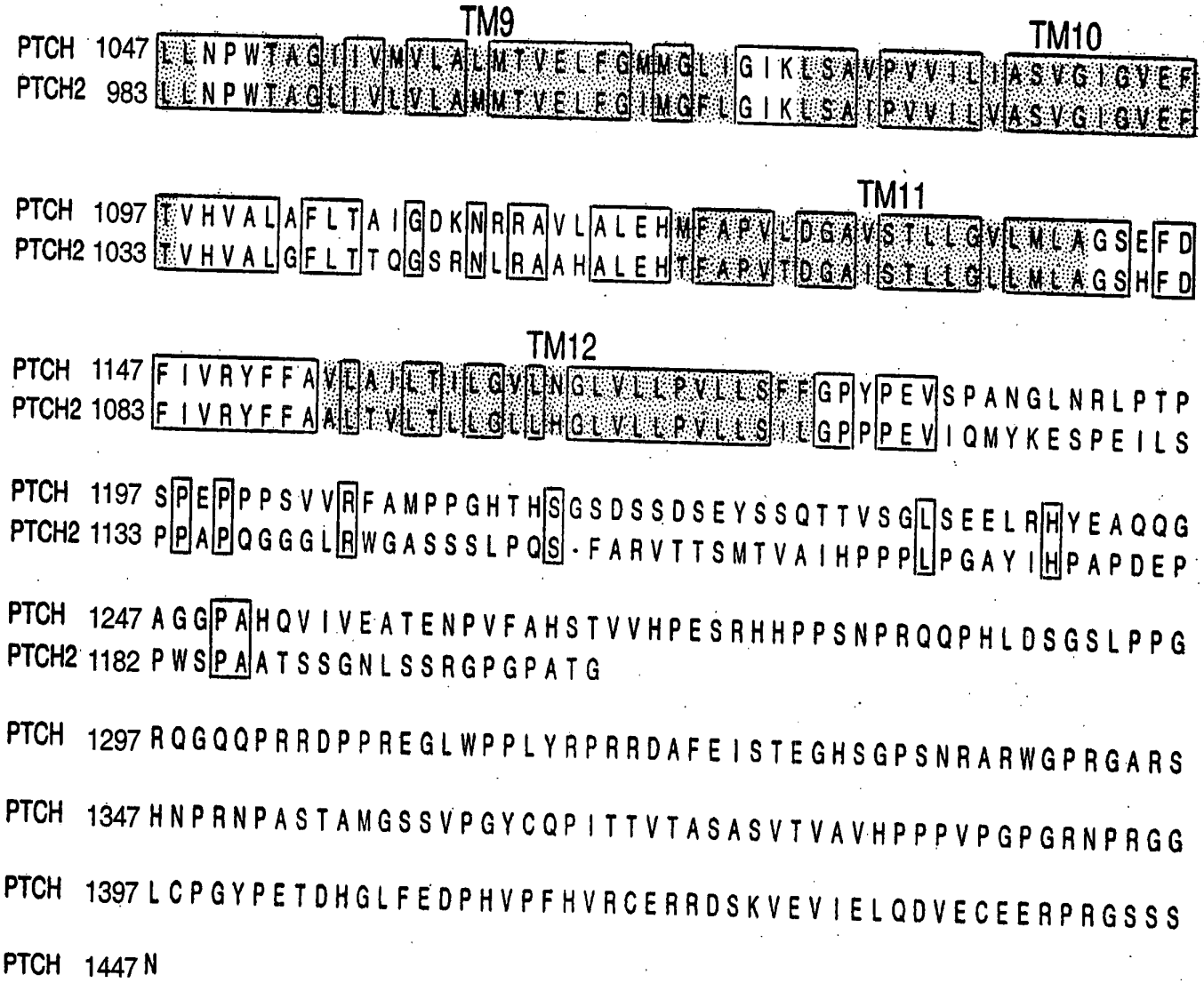
TM9
TM10
TM11
TM12
PTCH 1047 LLNPWTAGIIVMVLALMTVELFGMMGLIGIKLSAVPVVILIASVGIGVEF
PTCH2 983 LLNPWTAGLIVLVLAMMTVELFGIMGFLGIKLSAIPVVLLVASVGIGVEF
PTCH 1097 TVHVALAFLTAIGDKNRRAVLALEHMFAPVLDGAVSTLLGVLMLAGSEFD
PTCH2 1033 TVHVALGFLTTQGSRNLRAAHALEHTFAPVTDGAISTLLGLLMLAGSHFD
PTCH 1147 FIVRYFFAVLAILTILGVLNGLVLLPVLLSFFGPYPEVSPANGLNRLPTP
PTCH2 1083 FIVRYFFAALTVLTLLGLLHGLVLLPVLLSILGPPPEVIQMYKESPEILS
PTCH 1197 SPEPPPSVVRFAMPPGHTHSGSDSSDSEYSSQTTVSGLSEELRHYEAQQG
PTCH2 1133 PPAPQGGGLRWGASSSLPQS-FARVTTSMTVAIHPPPLPGAYIHPAPDEP
PTCH 1247 AGGPAHQVIVEATENPVFAHSTVVHPESRHHPPSNPRQQPHLDSGSLPPG
PTCH2 1182 PWSPAATSSGNLSSRGPGPATG
PTCH 1297 RQGQQPRRDPPREGLWPPLYRPRRDAFEISTEGHSGPSNRARWGPRGARS
PTCH 1347 HNPRNPASTAMGSSVPGYCQPITTVTASASVTVAVHPPPVPGPGRNPRGG
PTCH 1397 LCPGYPETDHGLFEDPHVPFHVRCERRDSKVEVIELQDVECEERPRGSSS
PTCH 1447 N

FIG._3D

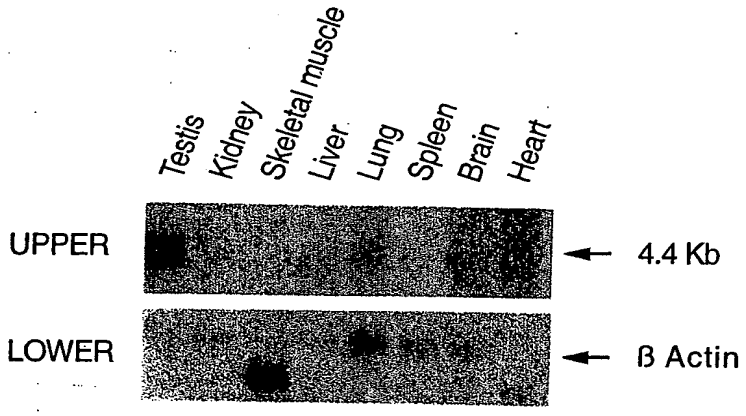
Testis
Kidney
Skeletal muscle
Liver
Lung
Spleen
Brain
Heart
UPPER
4.4 Kb
LOWER
ß Actin

FIG._4

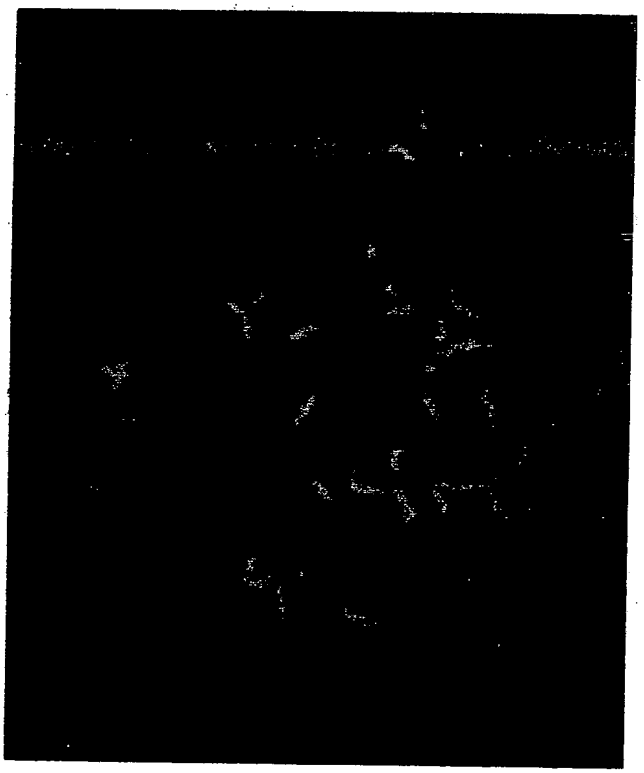

FIG._5

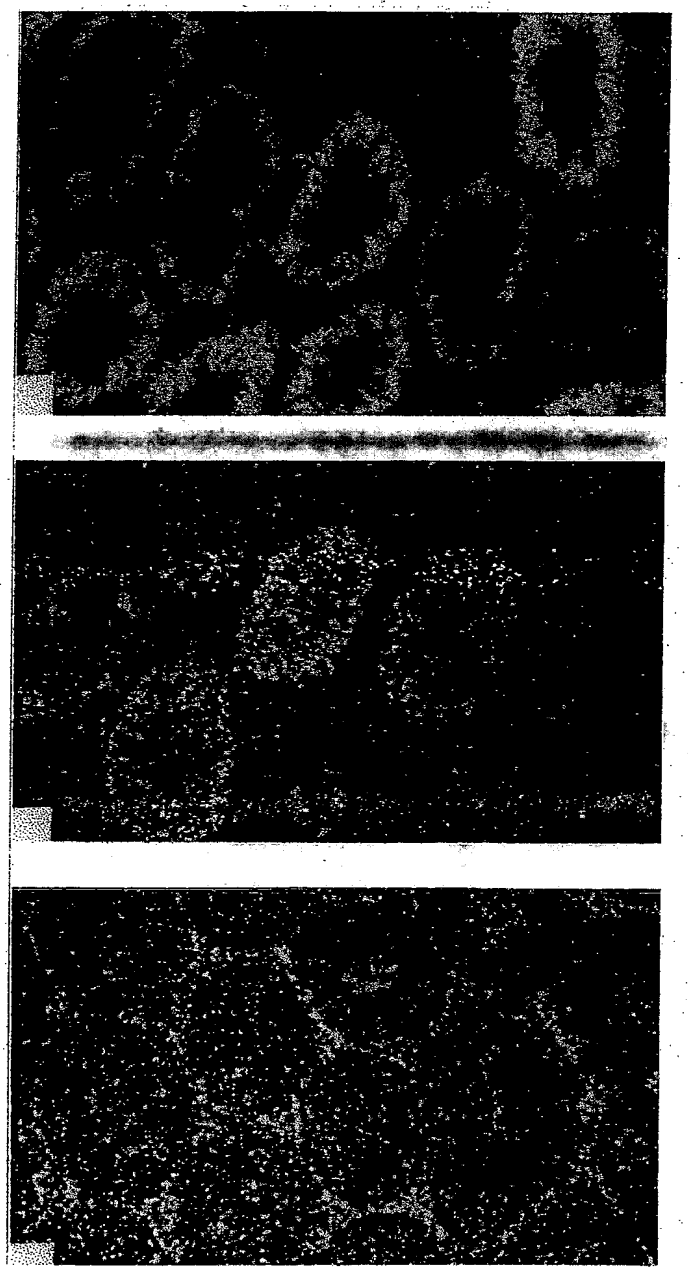

FIG._6C

FIG._6B

FIG._6A

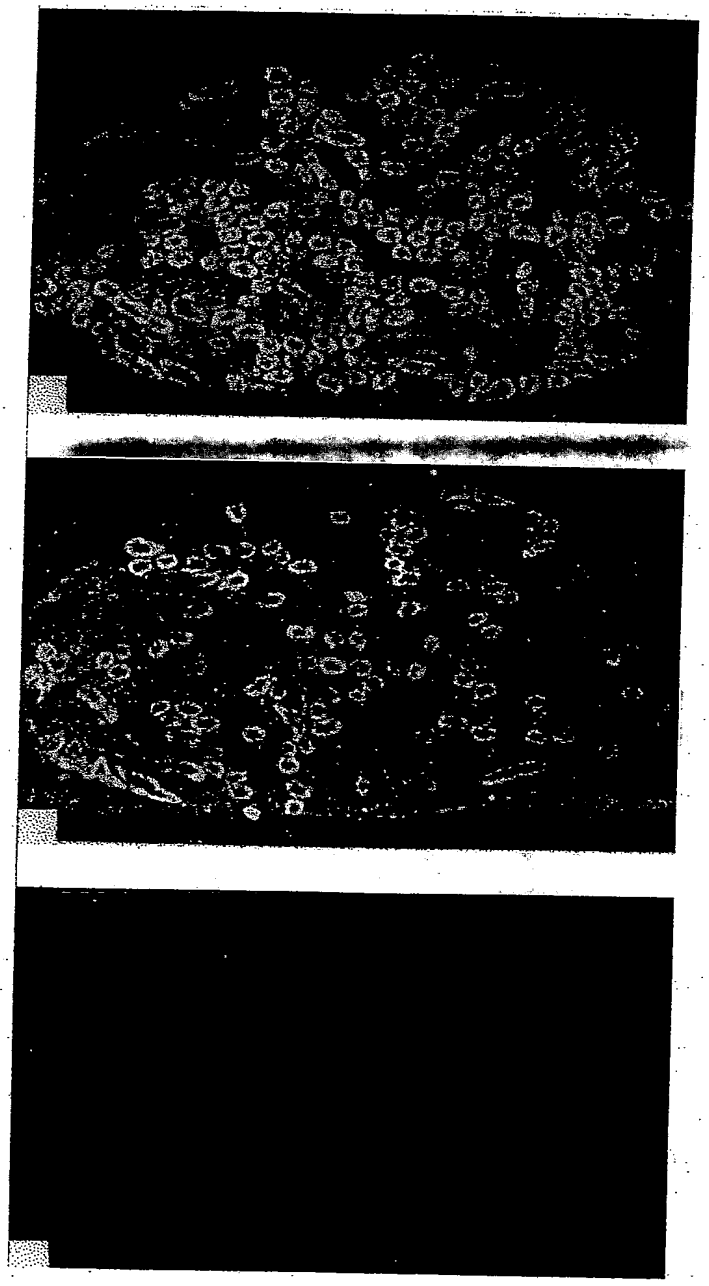

FIG._6F

FIG._6E

FIG._6D

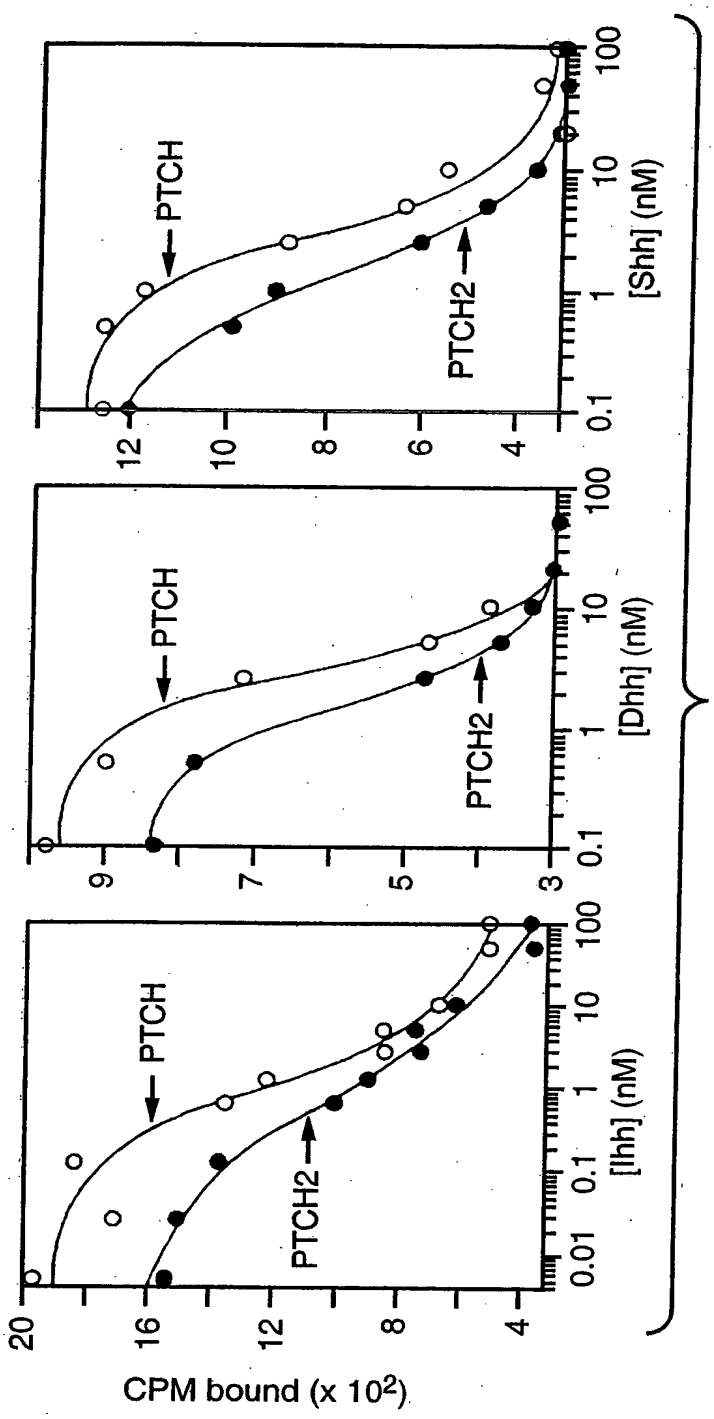

FIG._7A

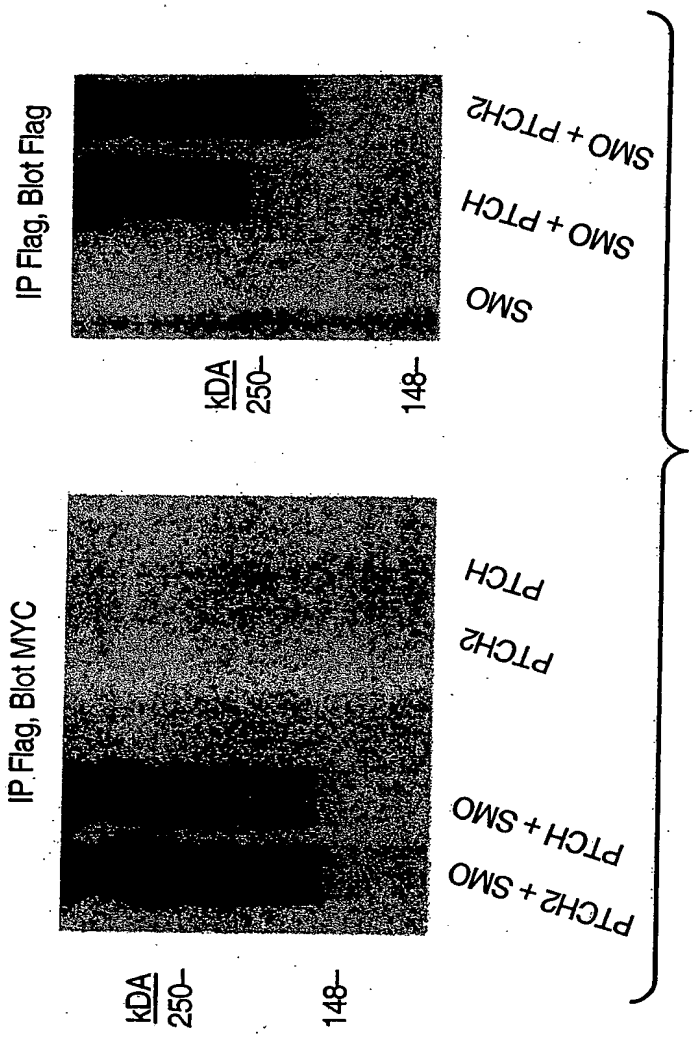
IP Flag, Blot Flag
SMO + PTCH2
SMO + PTCH
SMO
kDA
250-
148-
IP Flag, Blot MYC
PTCH
PTCH2
PTCH + SMO
PTCH2 + SMO
kDA
250-
148-

FIG._7B

```
                  10         20         30         40         50
hPtch-2   MTRSPPLRELPPSYTPPARTAAPQILAGSLKAPLWLRAYFQGLLFSLGCG
          * *. .* **********..**.******.******************
mPatched2 MVRPLSLGELPPSYTPPARSSAPHILAGSLQAPLWLRAYFQGLLFSLGCR
                  10         20         30         40         50

                  60         70         80         90         100
hPtch-2   IQRHCGKVLFLGLLAFGALALGLRMAIIETNLEQLWVEVGSRVSQELHYT
          **.**********.**********.*.***.******************
mPatched2 IQKHCGKVLFLGLVAFGALALGLRVAVIETDLEQLWVEVGSRVSQELHYT
                  60         70         80         90         100

                 110        120        130        140        150
hPtch-2   KEKLGEEAAYTSQMLIQTARQEGENILTPEALGLHLQAALTASKVQVSLY
          ******************.*** *.******.****************
mPatched2 KEKLGEEAAYTSQMLIQTAHQEGGNVLTPEALDLHLQAALTASKVQVSLY
                 110        120        130        140        150

                 160        170        180        190        200
hPtch-2   GKSWDLNKICYKSGVPLIENGMIEWMIEKLFPCVILTPLDCFWEGAKLQG
          ************************.************************
mPatched2 GKSWDLNKICYKSGVPLIENGMIERMIEKLFPCVILTPLDCFWEGAKLQG
                 160        170        180        190        200

                 210        220        230        240        250
hPtch-2   GSAYLPGRPDIQWTNLDPEQLLEELGPFASLEGFRELLDKAQVGQAYVGR
          ******************.********************************
mPatched2 GSAYLPGRPDIQWTNLDPQQLLEELGPFASLEGFRELLDKAQVGQAYVGR
                 210        220        230        240        250

                 260        270        280        290        300
hPtch-2   PCLHPDDLHCPPSAPNHHSRQAPNVAHELSGGCHGFSHKFMHWQEELLLG
          ***.*** ********.*********.************************
mPatched2 PCLDPDDPHCPPSAPNRHSRQAPNVAQELSGGCHGFSHKFMHWQEELLLG
                 260        270        280        290        300

                 310        320        330        340        350
hPtch-2   GMARDPQGELLRAEALQSTFLLMSPRQLYEHFRGDYQTHDIGWSEEQAST
          * *** **.****************************************
mPatched2 GTARDLQGQLLRAEALQSTFLLMSPRQLYEHFRGDYQTHDIGWSEEQASM
                 310        320        330        340        350
```

FIG._8A

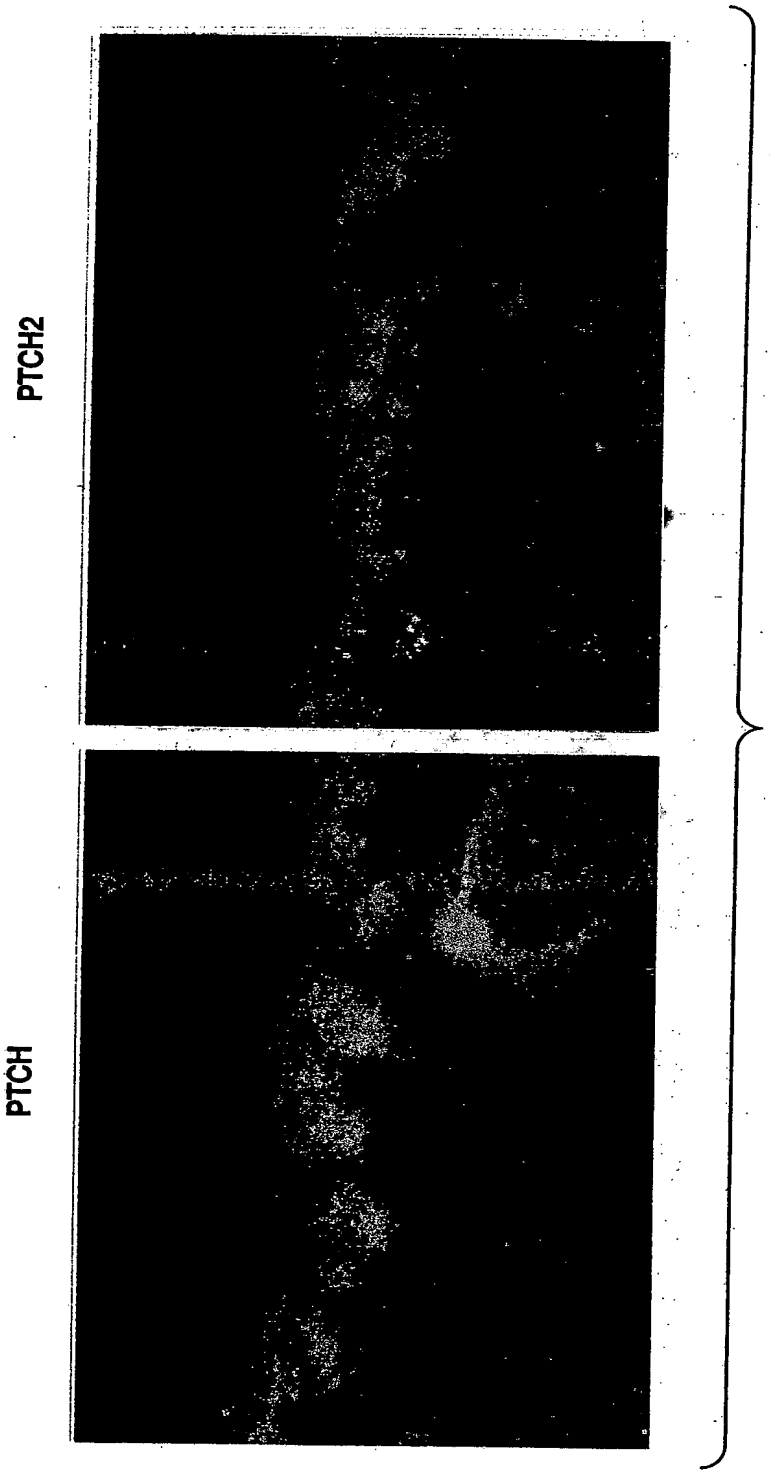

FIG._9

```
  1 CCCACGCGTC CGGGAGAAGC TGGGGGAGGA GGCTGCATAC ACCTCTCAGA TGCTGATACA GACCGCACGC CAGGAGGGAG AGAACATCCT CACACCCGAA
    GGGTGCGCAG GCCCTCTTCG ACCCCCTCCT CCGACGTATG TGGAGAGTCT ACGACTATGT CTGGCGTGCG GTCCTCCCTC TCTTGTAGGA GTGTGGGCTT

101 GCACTTGGCC TCCACCTCCA GGCAGCCCTC ACTGCCAGTA AAGTCCAAGT ATCACTCTAT GGGAAGTCCT GGGATTTGAA CAAAATCTGC TACAAGTCAG
    CGTGAACCGG AGGTGGAGGT CCGTCGGGAG TGACGGTCAT TTCAGGTTCA TAGTGAGATA CCCTTCAGGA CCCTAAACTT GTTTTAGACG ATGTTCAGTC

201 GAGTTCCCCT TATTGAAAAT GGAATGATTG AGCGGATGAT TGAGAAGCTG TTTCCGTGCG TGATCCTCAC CCCCCTCGAC TGCTTCTGGG AGGGAGCCAA
    CTCAAGGGGA ATAACTTTTA CCTTACTAAC TCGCCTACTA ACTCTTCGAC AAAGGCACGC ACTAGGAGTG GGGGGAGCTG ACGAAGACCC TCCCTCGGTT

301 ACTCCAAGGG GGCTCCGCCT ACCTGCCGCT CCCAATGTGG CTCACGAGCT GAGTGGGGGC TGCCATGGCT TCTCCCACAA ATTCATGCAC TGGCAGGAGG
    TGAGGTTCCC CCGAGGCGGA TGGACGGCGA GGGTTACACC GAGTGCTCGA CTCACCCCCG ACGGTACCGA AGAGGGTGTT TAAGTACGTG ACCGTCCTCC

401 AATTGCTGCT GGGAGGCATG GCCAGAGACC CCCAAGGAGA GCTGCTGAGG GCAGAGGCCC TGCAGAGCAC CTTCTTGCTG ATGAGTCCCC GCCAGCTGTA
    TTAACGACGA CCCTCCGTAC CGGTCTCTGG GGGTTCCTCT CGACGACTCC CGTCTCCGGG ACGTCTCGTG GAAGAACGAC TACTCAGGGG CGGTCGACAT

501 CGAGCATTTC CGGGGTGACT ATCAGACACA TGACATTGGC TGGAGTGAGG AGCAGGCCAG CACAGTGCTA CAAGCCTGGC AGCGGCGCTT TGTGCAGGTC
    GCTCGTAAAG GCCCCACTGA TAGTCTGTGT ACTGTAACCG ACCTCACTCC TCGTCCGGTC GTGTCACGAT GTTCGGACCG TCGCCGCGAA ACACGTCCAG

601 GGTATGGACA AGGACAGGGG GGTGCCCTGA GGCCATTCCC TCCTCCTGCC CCCTCCTATC CACCCTGTTT CTCCAGCTGG CCCAGGAGGC CCTGCCTGAG
    CCATACCTGT TCCTGTCCCC CCACGGGACT CCGGTAAGGG AGGAGGACGG GGGAGGATAG GTGGGACAAA GAGGTCGACC GGGTCCTCCG GGACGGACTC
```

FIG._10A

```
701 AACGCTTCCC AGCAGATCCA TGCCTTCTCC TCCACCACCC TGGATGACAT CCTGCATGCG TTCTCTGAAG TCAGTGCTGC CCGTGTGGTG GGAGGCTATC
    TTGCGAAGGG TCGTCTAGGT ACGGAAGAGG AGGTGGTGGG ACCTACTGTA GGACGTACGC AAGAGACTTC AGTCACGACG GGCACACCAC CCTCCGATAG

801 TGCTCATGGT GGGTCTTGCA CCTGGCACCT TGCCCCCACC CCACCTCCAA CCAGTGCCCA CCCTGGGGAG CCCCTGAGAC TGCCCTTTCC CCCCACAGCT
    ACGAGTACCA CCCAGAACGT GGACCGTGGA ACGGGGGTGG GGTGGAGGTT GGTCACGGGT GGGACCCCTC GGGGACTCTG ACGGGAAAGG GGGGTGTCGA

901 GGCCTATGCC TGTGTGACCA TGCTGCGGTG GGACTGCGCC CAGTCCCAGG GTTCCGTGGG CCTTGCCGGG GTACTGCTGG TGGCCCTGGC GGTGGCCTCA
    CCGGATACGG ACACACTGGT ACGACGCCAC CCTGACGCGG GTCAGGGTCC CAAGGCACCC GGAACGGCCC CATGACGACC ACCGGGACCG CCACCGGAGT

1001 GGCCTTGGGC TCTGTGCCCT GCTCGGCATC ACCTTCAATG CTGCCACTAC CCAGGTACGC CAGGACTGCA GGGCAGACTC AGTGCCAGTC ACCAGGCTTC
     CCGGAACCCG AGACACGGGA CGAGCCGTAG TGGAAGTTAC GACGGTGATG GGTCCATGCG GTCCTGACGT CCCGTCTGAG TCACGGTCAG TGGTCCGAAG

1101 ACGGGTCCTC AGCTGCCCGC TCCTCTGCCC CTCCAGGTGC TGCCCTTCTT GACTCTGGGA ATCGGCGTGG ATGACGTATT CCTGCTGGCG CATGCCTTCA
     TGCCCAGGAG TCGACGGGCG AGGAGACGGG GAGGTCCACG ACGGGAAGAA CTGAGACCCT TAGCCGCACC TACTGCATAA GGACGACCGC GTACGGAAGT

1201 CAGAGGCTCT GCCTGGCACC CCTCTCCAGG TGGGGCCTTG TCCCCCAGGG CTCATCTGAG GCAGCTCAGC TTACTGGTTA AGAGCCTCTT GGTTCAAGTG
     GTCTCCGAGA CGGACCGTGG GGAGAGGTCC ACCCCGGAAC AGGGGGTCCC GAGTAGACTC CGTCGAGTCG AATGACCAAT TCTCGGAGAA CCAAGTTCAC

1301 ACCTTGGGCT GCTAATGAAC CTCGGTGCCT CTTGTCCCCA TGTGTAAACA GGGGAAATAA TAGTGCTGTG TCCTAAGGGT TATTGTTTGG ATCAGTGAAG
     TGGAACCCGA CGATTACTTG GAGCCACGGA GAACAGGGGT ACACATTTGT CCCCTTTATT ATCACGACAC AGGATTCCCA ATAACAAACC TAGTCACTTC

1401 TAACTCAAGT TGAATGCTTA GAACAGCCCA TCATACGTAC ATGGTACCCA ATAAATGCTA GCCACTGTGT TATGACTGCC CCACCTCTGC ACCCCAAGTT
     ATTGAGTTCA ACTTACGAAT CTTGTCGGGT AGTATGCATG TACCATGGGT TATTTACGAT CGGTGACACA ATACTGACGG GGTGGAGACG TGGGGTTCAA
```

FIG._10B

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1501 CCTGAGCCTC CCCTTCACTC CACTTTGACA CGGCCCCTCC CTTGTGACCT GAGGGCAGGT CCCCACTCTG TCCTGGCAGG AGCGCATGGG CGAGTGTCTG
     GGACTCGGAG GGGAAGTGAG GTGAAACTGT GCCGGGGAGG GAACACTGGA CTCCCGTCCA GGGGTGAGAC AGGACCGTCC TCGCGTACCC GCTCACAGAC

1601 CAGCGCACGG GCACCAGTGT TGTACTCACA TCCATCAACA ACATGGCCGC CTTCCTCATG GCTGCCCTCG TTCCCATCCC TGCGCTGCGA GCCTTCTCCC
     GTCGCGTGCC CGTGGTCACA ACATGAGTGT AGGTAGTTGT TGTACCGGCG GAAGGAGTAC CGACGGGAGC AAGGGTAGGG ACGCGACGCT CGGAAGAGGG

1701 TACAGCCTGG ACCTACGGCG GCGCCACTGC CAGCGCCTTG ATGTGCTCTG CTGCTTCTCC AGGTACTGCC TGCGCCCCAG CCCCTTCCTC CCGTGACCCA
     ATGTCGGACC TGGATGCCGC CGCGGTGACG GTCGCGGAAC TACACGAGAC GACGAAGAGG TCCATGACGG ACGCGGGGTC GGGGAAGGAG GGCACTGGGT

1801 CGCCAGCCTG TCCCCTCACC AGCATTTCAA GGCACAGACC TGTCATCCAC TCTCTACCTC TTCCAGTCCC TGCTCTGCTC AGGTGATTCA GATCCTGCCC
     GCGGTCGGAC AGGGGAGTGG TCGTAAAGTT CCGTGTCTGG ACAGTAGGTG AGAGATGGAG AAGGTCAGGG ACGAGACGAG TCCACTAAGT CTAGGACGGG

1901 CAGGAGCTGG GGGACGGGAC AGTACCAGTG GGCATTGCCC ACCTCACTGC CACAGTTCAA GCCTTTACCC ACTGTGAAGC CAGCAGCCAG CATGTGGTCA
     GTCCTCGACC CCCTGCCCTG TCATGGTCAC CCGTAACGGG TGGAGTGACG GTGTCAAGTT CGGAAATGGG TGACACTTCG GTCGTCGGTC GTACACCAGT

2001 CCATCCTGCC TCCCCAAGCC CACCTGGTGC CCCCACCTTC TGACCCACTG GGCTCTGAGC TCTTCAGCCC TGGAGGGTCC ACACGGGACC TTCTAGGCCA
     GGTAGGACGG AGGGGTTCGG GTGGACCACG GGGGTGGAAG ACTGGGTGAC CCGAGACTCG AGAAGTCGGG ACCTCCCAGG TGTGCCCTGG AAGATCCGGT

2101 GGAGGAGGAG ACAAGGCAGA AGGCAGCCTG CAAGTCCCTG CCCTGTGCCC GCTGGAATCT TGCCCATTTC GCCCGCTATC AGTTTGCCCC GTTGCTGCTC
     CCTCCTCCTC TGTTCCGTCT TCCGTCGGAC GTTCAGGGAC GGGACACGGG CGACCTTAGA ACGGGTAAAG CGGGCGATAG TCAAACGGGG CAACGACGAG

2201 CAGTCACATG CCAAGGCCAT CGTGCTGGTG CTCTTTGGTG CTCTTCTGGG CCTGAGCCTC TACGGAGCCA CCTTGGTGCA AGACGGCCTG GCCCTGACGG
     GTCAGTGTAC GGTTCCGGTA GCACGACCAC GAGAAACCAC GAGAAGACCC GGACTCGGAG ATGCCTCGGT GGAACCACGT TCTGCCGGAC CGGGACTGCC
```

FIG._10C

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2301 ATGTGGTGCC TCGGGGCACC AAGGAGCATG CCTTCCTGAG CGCCCAGCTC AGGTACTTCT CCCTGTACGA GGTGGCCCTG GTGACCCAGG GTGGCTTTGA
     TACACCACGG AGCCCCGTGG TTCCTCGTAC GGAAGGACTC GCGGGTCGAG TCCATGAAGA GGGACATGCT CCACCGGGAC CACTGGGTCC CACCGAAACT

2401 CTACGCCCAC TCCCAACGCG CCCTCTTTGA TCTGCACCAG CGCTTCAGTT CCCTCAAGGC GGTGCTGCCC CCACCGGCCA CCCAGGCACC CCGCACCTGG
     GATGCGGGTG AGGGTTGCGC GGGAGAAACT AGACGTGGTC GCGAAGTCAA GGGAGTTCCG CCACGACGGG GGTGGCCGGT GGGTCCGTGG GGCGTGGACC

2501 CTGCACTATT ACCGCAACTG GCTACAGGGA ATCCAGGCTG CCTTTGACCA GGACTGGGCT TCTGGGCGCA TCACCCGCCA CTCGTACCGC AATGGCTCTG
     GACGTGATAA TGGCGTTGAC CGATGTCCCT TAGGTCCGAC GGAAACTGGT CCTGACCCGA AGACCCGCGT AGTGGGCGGT GAGCATGGCG TTACCGAGAC

2601 AGGATGGGGC CCTGGCCTAC AAGCTGCTCA TCCAGACTGG AGACGCCCAG GAGCCTCTGG ATTTCAGCCA GGTTGGGAGA GGGCTGGAGG GGTCCACTAG
     TCCTACCCCG GGACCGGATG TTCGACGAGT AGGTCTGACC TCTGCGGGTC CTCGGAGACC TAAAGTCGGT CCAACCCTCT CCCGACCTCC CCAGGTGATC

2701 TACAGGGGCT GCAGGCCTCC TGGGCCCAGG CCTTCAGCCC TCTCTGCCTC TGCAGCTGAC CACAAGGAAG CTGGTGGACA GAGAGGGACT GATTCCACCC
     ATGTCCCCGA CGTCCGGAGG ACCCGGGTCC GGAAGTCGGG AGAGACGGAG ACGTCGACTG GTGTTCCTTC GACCACCTGT CTCTCCCTGA CTAAGGTGGG

2801 GAGCTCTTCT ACATGGGGCT GACCGTGTGG GTGAGCAGTG ACCCCCTGGG TCTGGCAGCC TCACAGGCCA ACTTCTACCC CCCACCTCCT GAATGGCTGC
     CTCGAGAAGA TGTACCCCGA CTGGCACACC CACTCGTCAC TGGGGGACCC AGACCGTCGG AGTGTCCGGT TGAAGATGGG GGGTGGAGGA CTTACCGACG

2901 ACGACAAATA CGACACCACG GGGGAGAACC TTCGCAGTGA GTCTTGGGGG GAGCTCGGCA AGAGCCTCAG CCTCGCCCAC ACAAGCCCTG AGCCTGAGGC
     TGCTGTTTAT GCTGTGGTGC CCCCTCTTGG AAGCGTCACT CAGAACCCCC CTCGAGCCGT TCTCGGAGTC GGAGCGGGTG TGTTCGGGAC TCGGACTCCG

3001 CCTGCCCACT CTGCCCCGTG CTCACCGCCC TGTCCCTCTC CCTCTTCTCC CTTCCCCTCC CCTCCACAGT CCCGCCAGCT CAGCCCTTGG AGTTTGCCCA
     GGACGGGTGA GACGGGGCAC GAGTGGCGGG ACAGGGAGAG GGAGAAGAGG GAAGGGGAGG GGAGGTGTCA GGGCGGTCGA GTCGGGAACC TCAAACGGGT
```

FIG._10D

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3101 GTTCCCCTTC CTGCTGCGTG GCCTCCAGAA GACTGCAGAC TTTGTGGAGG CCATCGAGGG GGCCCGGGCA GCATGCGCAG AGGCCGGCCA GGCTGGGGTG
     CAAGGGGAAG GACGACGCAC CGGAGGTCTT CTGACGTCTG AAACACCTCC GGTAGCTCCC CCGGGCCCGT CGTACGCGTC TCCGGCCGGT CCGACCCCAC

3201 CACGCCTACC CCAGCGGCTC CCCCTTCCTC TTCTGGGAAC AGTATCTGGG CCTGCGGCGC TGCTTCCTGC TGGCCGTCTG CATCCTGCTG GTGTGCACTT
     GTGCGGATGG GGTCGCCGAG GGGGAAGGAG AAGACCCTTG TCATAGACCC GGACGCCGCG ACGAAGGACG ACCGGCAGAC GTAGGACGAC CACACGTGAA

3301 TCCTCGTCTG TGCTCTGCTG CTCCTCAACC CCTGGACGGC TGGCCTCATA GTGAGTGCTT GCAGGAGTGG GGACAGAGAC ACCCCACCCT TCCCTGCCCA
     AGGAGCAGAC ACGAGACGAC GAGGAGTTGG GGACCTGCCG ACCGGAGTAT CACTCACGAA CGTCCTCACC CCTGTCTCTG TGGGGTGGGA AGGGACGGGT

3401 GCCTGTCATC CCTCCTGCCA GGAGCCCTCT GTGAGCCCTG TCTCCCTCAG GTGCTGGTCC TGGCGATGAT GACAGTGGAA CTCTTTGGTA TCATGGGTTT
     CGGACAGTAG GGAGGACGGT CCTCGGGAGA CACTCGGGAC AGAGGGAGTC CACGACCAGG ACCGCTACTA CTGTCACCTT GAGAAACCAT AGTACCCAAA

3501 CCTGGGCATC AAGCTGAGTG CCATCCCCGT GGTGATCCTT GTGGCCTCTG TAGGCATTGG CGTTGAGTTC ACAGTCCACG TGGCTCTGGT GAGCACGGGC
     GGACCCGTAG TTCGACTCAC GGTAGGGGCA CCACTAGGAA CACCGGAGAC ATCCGTAACC GCAACTCAAG TGTCAGGTGC ACCGAGACCA CTCGTGCCCG

3601 ACCCCGGGGA GGGACCAATC AGCTGATTCA GTATTCAACA CATATTGTTC AAGCCCCTAC TATGTGCTAG GTACTATTTA AGAATTTGGG CTGGGTGGAC
     TGGGGCCCCT CCCTGGTTAG TCGACTAAGT CATAAGTTGT GTATAACAAG TTCGGGGATG ATACACGATC CATGATAAAT TCTTAAACCC GACCCACCTG

3701 GTGGTGGCTC ATTCCTGTAA TCCCAGCACT TTGGGAGGCC GAGGCGGGTG GATCACCTGA GGTCGGGAGT TCGAAACCAG CCTGGCCAAC ATGGTGAAAC
     CACCACCGAG TAAGGACATT AGGGTCGTGA AACCCTCCGG CTCCGCCCAC CTAGTGGACT CCAGCCCTCA AGCTTTGGTC GGACCGGTTG TACCACTTTG

3801 CCTGTCTTTA CTAAAAATAC AAAAAATTAG CCAGGCGTGG TGGCACATGC CAGTAGTCCC AGCTACTTTG GAGGCTGAGG CAGAATTGCT TGAACCTGGG
     GGACAGAAAT GATTTTTATG TTTTTTAATC GGTCCGCACC ACCGTGTACG GTCATCAGGG TCGATGAAAC CTCCGACTCC GTCTTAACGA ACTTGGACCC

3901 AGGCGAAGGT TGCAGTGAGC TGAGATCGTG CCATTGCACT CCAGCCTGGG CAACAAGAGT GCAACTCTCC GTCTCAAAAA AAAAAAAAAA AAGGGCGGCC
     TCCGCTTCCA ACGTCACTCG ACTCTAGCAC GGTAACGTGA GGTCGGACCC GTTGTTCTCA CGTTGAGAGG CAGAGTTTTT TTTTTTTTTT TTCCCGCCGG

4001 GCGA
     CGCT
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FIG._10E

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  1 TTCCGGCATG ACTCGATCGC CGCCCCTCAG AGAGCTGCCC CCGAGTTACA CACCCCCAGC TCGAACCGCA GCACCCCAGA TCCTAGCTGG GAGCCTGAAG
    AAGGCCGTAC TGAGCTAGCG GCGGGGAGTC TCTCGACGGG GGCTCAATGT GTGGGGGTCG AGCTTGGCGT CGTGGGGTCT AGGATCGACC CTCGGACTTC

101 GCTCCACTCT GGCTTCGTGC TTACTTCCAG GGCCTGCTCT TCTCTCTGGG ATGCGGGATC CAGAGACATT GTGGCAAAGT GCTCTTTCTG GGACTGTTGG
    CGAGGTGAGA CCGAAGCACG AATGAAGGTC CCGGACGAGA AGAGAGACCC TACGCCCTAG GTCTCTGTAA CACCGTTTCA CGAGAAAGAC CCTGACAACC

201 CCTTTGGGGC CCTGGCATTA GGTCTCCGCA TGGCCATTAT TGAGACAAAC TTGGAACAGC TCTGGGTAGA AGTGGGCAGC CGGGTGAGCC AGGAGCTGCA
    GGAAACCCCG GGACCGTAAT CCAGAGGCGT ACCGGTAATA ACTCTGTTTG AACCTTGTCG AGACCCATCT TCACCCGTCG GCCCACTCGG TCCTCGACGT

301 TTACACCAAG GAGAAGCTGG GGGAGGAGGC TGCATACACC TCTCAGATGC TGATACAGAC CGCACGCCAG GAGGGAGAGA ACATCCTCAC ACCCGAAGCA
    AATGTGGTTC CTCTTCGACC CCCTCCTCCG ACGTATGTGG AGAGTCTACG ACTATGTCTG GCGTGCGGTC CTCCCTCTCT TGTAGGAGTG TGGGCTTCGT

401 CTTGGCCTCC ACCTCCAGGC AGCCCTCACT GCCAGTAAAG TCCAAGTATC ACTCTATGGG AAGTCCTGGG ATTTGAACAA AATCTGCTAC AAGTCAGGAG
    GAACCGGAGG TGGAGGTCCG TCGGGAGTGA CGGTCATTTC AGGTTCATAG TGAGATACCC TTCAGGACCC TAAACTTGTT TTAGACGATG TTCAGTCCTC

501 TTCCCCTTAT TGAAAATGGA ATGATTGAGT GGATGATTGA GAAGCTGTTT CCGTGCGTGA TCCTCACCCC CCTCGACTGC TTCTGGGAGG GAGCCAAACT
    AAGGGGAATA ACTTTTACCT TACTAACTCA CCTACTAACT CTTCGACAAA GGCACGCACT AGGAGTGGGG GGAGCTGACG AAGACCCTCC CTCGGTTTGA
```

FIG._11A

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601 CCAAGGGGGC TCCGCCTACC TGCCCGGCCG CCCGGATATC CAGTGGACCA ACCTGGATCC AGAGCAGCTG CTGGAGGAGC TGGGTCCCTT TGCCTCCCTT
    GGTTCCCCCG AGGCGGATGG ACGGGCCGGC GGGCCTATAG GTCACCTGGT TGGACCTAGG TCTCGTCGAC GACCTCCTCG ACCCAGGGAA ACGGAGGGAA

701 GAGGGCTTCC GGGAGCTGCT AGACAAGGCA CAGGTGGGCC AGGCCTACGT GGGGCGGCCC TGTCTGCACC CTGATGACCT CCACTGCCCA CCTAGTGCCC
    CTCCCGAAGG CCCTCGACGA TCTGTTCCGT GTCCACCCGG TCCGGATGCA CCCCGCCGGG ACAGACGTGG GACTACTGGA GGTGACGGGT GGATCACGGG

801 CCAACCATCA CAGCAGGCAG GCTCCCAATG TGGCTCACGA GCTGAGTGGG GGCTGCCATG GCTTCTCCCA CAAATTCATG CACTGGCAGG AGGAATTGCT
    GGTTGGTAGT GTCGTCCGTC CGAGGGTTAC ACCGAGTGCT CGACTCACCC CCGACGGTAC CGAAGAGGGT GTTTAAGTAC GTGACCGTCC TCCTTAACGA

901 GCTGGGAGGC ATGGCCAGAG ACCCCCAAGG AGAGCTGCTG AGGGCAGAGG CCCTGCAGAG CACCTTCTTG CTGATGAGTC CCCGCCAGCT GTACGAGCAT
    CGACCCTCCG TACCGGTCTC TGGGGGTTCC TCTCGACGAC TCCCGTCTCC GGGACGTCTC GTGGAAGAAC GACTACTCAG GGGCGGTCGA CATGCTCGTA

1001 TTCCGGGGTG ACTATCAGAC ACATGACATT GGCTGGAGTG AGGAGCAGGC CAGCACAGTG CTACAAGCCT GGCAGCGGCG CTTTGTGCAG CTGGCCCAGG
     AAGGCCCCAC TGATAGTCTG TGTACTGTAA CCGACCTCAC TCCTCGTCCG GTCGTGTCAC GATGTTCGGA CCGTCGCCGC GAAACACGTC GACCGGGTCC

1101 AGGCCCTGCC TGAGAACGCT TCCCAGCAGA TCCATGCCTT CTCCTCCACC ACCCTGGATA ACATCCTGCA TGCGTTCTCT GAAGTCAGTG CTGCCCGTGT
     TCCGGGACGG ACTCTTGCGA AGGGTCGTCT AGGTACGGAA GAGGAGGTGG TGGGACCTAT TGTAGGACGT ACGCAAGAGA CTTCAGTCAC GACGGGCACA

1201 GGTGGGAGGC TATCTGCTCA TGCTGGCCTA TGCCTGTGTG ACCATGCTGC GGTGGGACTG CGCCCAGTCC CAGGGTTCCG TGGGCCTTGC CGGGGTACTG
     CCACCCTCCG ATAGACGAGT ACGACCGGAT ACGGACACAC TGGTACGACG CCACCCTGAC GCGGGTCAGG GTCCCAAGGC ACCCGGAACG GCCCCATGAC

1301 CTGGTGGCCC TGGCGGTGGC CTCAGGCCTT GGGCTCTGTG CCCTGCTCGG CATCACCTTC AATGCTGCCA CTACCCAGGT GCTGCCCTTC TTGGCTCTGG
     GACCACCGGG ACCGCCACCG GAGTCCGGAA CCCGAGACAC GGGACGAGCC GTAGTGGAAG TTACGACGGT GATGGGTCCA CGACGGGAAG AACCGAGACC
```

FIG._11B

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1401 GAATCGGCGT GGATGACGTA TTCCTGCTGG CGCATGCCTT CACAGAGGCT CTGCCTGGCA CCCCTCTCCA GGAGCGCATG GGCGAGTGTC TGCAGCGCAC
     CTTAGCCGCA CCTACTGCAT AAGGACGACC GCGTACGGAA GTGTCTCCGA GACGGACCGT GGGGAGAGGT CCTCGCGTAC CCGCTCACAG ACGTCGCGTG

1501 GGGCACCAGT GTCGTACTCA CATCCATCAA CAACATGGCC GCCTTCCTCA TGGCTGCCCT CGTTCCCATC CCTGCGCTGC GAGCCTTCTC CTTACAGCCA
     CCCGTGGTCA CAGCATGAGT GTAGGTAGTT GTTGTACCGG CGGAAGGAGT ACCGACGGGA GCAAGGGTAG GGACGCGACG CTCGGAAGAG GAATGTCGGT

1601 TCCTCAGCCT GGACCTACGG CGGCGCCACT GCCAGCGCCT TGATGTGCTC TGCTGCTTCT CCAGTCCCTG CTCTGCTCAG GTGATTCAGA TCCTGCCCCA
     AGGAGTCGGA CCTGGATGCC GCCGCGGTGA CGGTCGCGGA ACTACACGAG ACGACGAAGA GGTCAGGGAC GAGACGAGTC CACTAAGTCT AGGACGGGGT

1701 GGAGCTGGGG GACGGGACAG TACCAGTGGG CATTGCCCAC CTCACTGCCA CAGTTCAAGC CTTTACCCAC TGTGAAGCCA GCAGCCAGCA TGTGGTCACC
     CCTCGACCCC CTGCCCTGTC ATGGTCACCC GTAACGGGTG GAGTGACGGT GTCAAGTTCG GAAATGGGTG ACACTTCGGT CGTCGGTCGT ACACCAGTGG

1801 ATCCTGCCTC CCCAAGCCCA CCTGGTGCCC CCACCTTCTG ACCCACTGGG CTCTGAGCTC TTCAGCCCTG GAGGGTCCAC ACGGGACCTT CTAGGCCAGG
     TAGGACGGAG GGGTTCGGGT GGACCACGGG GGTGGAAGAC TGGGTGACCC GAGACTCGAG AAGTCGGGAC CTCCCAGGTG TGCCCTGGAA GATCCGGTCC

1901 AGGAGGAGAC AAGGCAGAAG GCAGCCTGCA AGTCCCTGCC CTGTGCCCGC TGGAATCTTG CCCATTTCGC CCCGGAATTC CTGCAGCCCG GGGGATCCAC
     TCCTCCTCTG TTCCGTCTTC CGTCGGACGT TCAGGGACGG GACACGGGCG ACCTTAGAAC GGGTAAAGCG GGGCCTTAAG GACGTCGGGC CCCCTAGGTG

2001 TAGTTCTAGA GCGGCCGCCA CCGCGGTGGA GCTCCAGCTT TTGTTCCCTT TAGTGAGGGT TAATTGCGCG CTTGGGTATC TT
     ATCAAGATCT CGCCGGCGGT GGCGCCACCT CGAGGTCGAA AACAAGGGAA ATCACTCCCA ATTAACGCGC GAACCCATAG AA
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FIG._11C

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  1 GTTATTTCAG GCCATGGTGT TGCGCCGAAT TAATTCCCGA TCCAGACATG ATAAGATACA TTGATGAGTT TGGACAAACC ACAACTAGAA TGCAGTGAAA
    CAATAAAGTC CGGTACCACA ACGCGGCTTA ATTAAGGGCT AGGTCTGTAC TATTCTATGT AACTACTCAA ACCTGTTTGG TGTTGATCTT ACGTCACTTT
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~~(SEQ ID NO: 1)~~

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101 AAAATGCTTT ATTTGTGAAA TTTGTGATGC TATTGCTTTA TTTGTAACCA TTATAAGCTG CAATAAACAA GTTGGGCCAT GGCGGCCAAG CTTCTGCAGG
    TTTTACGAAA TAAACACTTT AAACACTACG ATAACGAAAT AAACATTGGT AATATTCGAC GTTATTTGTT CAACCCGGTA CCGCCGGTTC GAAGACGTCC

201 TCGACTCTAG AGGATCCCCG GGGAATTCCG GCATGACTCG ATCGCCGCCC CTCAGAGAGC TGCCCCCGAG TTACACACCC CCAGCTCGAA CCGCAGCACC
    AGCTGAGATC TCCTAGGGGC CCCTTAAGGC CGTACTGAGC TAGCGGCGGG GAGTCTCTCG ACGGGGGCTC AATGTGTGGG GGTCGAGCTT GGCGTCGTGG
  1                                 M  T  R  S  P  P  L  R  E  L  P  P  S  Y  T  P  P  A  R  T  A  A  P
```

~~^insert starts here~~ ~~(SEQ ID NO: 2)~~

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301 CCAGATCCTA GCTGGGAGCC TGAAGGCTCC ACTCTGGCTT CGTGCTTACT TCCAGGGCCT GCTCTTCTCT CTGGGATGCG GGATCCAGAG ACATTGTGGC
    GGTCTAGGAT CGACCCTCGG ACTTCCGAGG TGAGACCGAA GCACGAATGA AGGTCCCGGA CGAGAAGAGA GACCCTACGC CCTAGGTCTC TGTAACACCG
 24 Q  I  L  A  G  S  L  K  A  P  L  W  L  R  A  Y  F  Q  G  L  L  F  S  L  G  C  G  I  Q  R  H  C  G

401 AAAGTGCTCT TTCTGGGACT GTTGGCCTTT GGGGCCCTGG CATTAGGTCT CCGCATGGCC ATTATTGAGA CAAACTTGGA ACAGCTCTGG GTAGAAGTGG
    TTTCACGAGA AAGACCCTGA CAACCGGAAA CCCCGGGACC GTAATCCAGA GGCGTACCGG TAATAACTCT GTTTGAACCT TGTCGAGACC CATCTTCACC
 57 K  V  L  F  L  G  L  L  A  F  G  A  L  A  L  G  L  R  M  A  I  I  E  T  N  L  E  Q  L  W  V  E  V  G

501 GCAGCCGGGT GAGCCAGGAG CTGCATTACA CCAAGGAGAA GCTGGGGGAG GAGGCTGCAT ACACCTCTCA GATGCTGATA CAGACCGCAC GCCAGGAGGG
    CGTCGGCCCA CTCGGTCCTC GACGTAATGT GGTTCCTCTT CGACCCCCTC CTCCGACGTA TGTGGAGAGT CTACGACTAT GTCTGGCGTG CGGTCCTCCC
 91   S  R  V  S  Q  E  L  H  Y  T  K  E  K  L  G  E  E  A  A  Y  T  S  Q  M  L  I  Q  T  A  R  Q  E  G

601 AGAGAACATC CTCACACCCG AAGCACTTGG CCTCCACCTC CAGGCAGCCC TCACTGCCAG TAAAGTCCAA GTATCACTCT ATGGGAAGTC CTGGGATTTG
    TCTCTTGTAG GAGTGTGGGC TTCGTGAACC GGAGGTGGAG GTCCGTCGGG AGTGACGGTC ATTTCAGGTT CATAGTGAGA TACCCTTCAG GACCCTAAAC
124 E  N  I  L  T  P  E  A  L  G  L  H  L  Q  A  A  L  T  A  S  K  V  Q  V  S  L  Y  G  K  S  W  D  L

701 AACAAAATCT GCTACAAGTC AGGAGTTCCC CTTATTGAAA ATGGAATGAT TGAGTGGATG ATTGAGAAGC TGTTTCCGTG CGTGATCCTC ACCCCCCTCG
    TTGTTTTAGA CGATGTTCAG TCCTCAAGGG GAATAACTTT TACCTTACTA ACTCACCTAC TAACTCTTCG ACAAAGGCAC GCACTAGGAG TGGGGGGAGC
157 N  K  I  C  Y  K  S  G  V  P  L  I  E  N  G  M  I  E  W  M  I  E  K  L  F  P  C  V  I  L  T  P  L  D

801 ACTGCTTCTG GGAGGGAGCC AAACTCCAAG GGGGCTCCGC CTACCTGCCC GGCCGCCCGG ATATCCAGTG GACCAACCTG GATCCAGAGC AGCTGCTGGA
    TGACGAAGAC CCTCCCTCGG TTTGAGGTTC CCCCGAGGCG GATGGACGGG CCGGCGGGCC TATAGGTCAC CTGGTTGGAC CTAGGTCTCG TCGACGACCT
191   C  F  W  E  G  A  K  L  Q  G  G  S  A  Y  L  P  G  R  P  D  I  Q  W  T  N  L  D  P  E  Q  L  L  E
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FIG. 1A

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901 GGAGCTGGGT CCCTTTGCCT CCCTTGAGGG CTTCCGGGAG CTGCTAGACA AGGCACAGGT GGGCCAGGCC TACGTGGGGC GGCCCTGTCT GCACCCTGAT
    CCTCGACCCA GGGAAACGGA GGGAACTCCC GAAGGCCCTC GACGATCTGT TCCGTGTCCA CCCGGTCCGG ATGCACCCCG CCGGGACAGA CGTGGGACTA
224  E  L  G  P  F  A  S  L  E  G  F  R  E  L  L  D  K  A  Q  V  G  Q  A  Y  V  G  R  P  C  L  H  P  D

1001 GACCTCCACT GCCCACCTAG TGCCCCCAAC CATCACAGCA GGCAGGCTCC CAATGTGGCT CACGAGCTGA GTGGGGGCTG CCATGGCTTC TCCCACAAAT
    CTGGAGGTGA CGGGTGGATC ACGGGGGTTG GTAGTGTCGT CCGTCCGAGG GTTACACCGA GTGCTCGACT CACCCCCGAC GGTACCGAAG AGGGTGTTTA
257  D  L  H  C  P  P  S  A  P  N  H  H  S  R  Q  A  P  N  V  A  H  E  L  S  G  G  C  H  G  F  S  H  K  F

1101 TCATGCACTG GCAGGAGGAA TTGCTGCTGG GAGGCATGGC CAGAGACCCC CAAGGAGAGC TGCTGAGGGC AGAGGCCCTG CAGAGCACCT TCTTGCTGAT
    AGTACGTGAC CGTCCTCCTT AACGACGACC CTCCGTACCG GTCTCTGGGG GTTCCTCTCG ACGACTCCCG TCTCCGGGAC GTCTCGTGGA AGAACGACTA
291   M  H  W  Q  E  E  L  L  L  G  G  M  A  R  D  P  Q  G  E  L  L  R  A  E  A  L  Q  S  T  F  L  L  M

1201 GAGTCCCCGC CAGCTGTACG AGCATTTCCG GGGTGACTAT CAGACACATG ACATTGGCTG GAGTGAGGAG CAGGCCAGCA CAGTGCTACA AGCCTGGCAG
    CTCAGGGGCG GTCGACATGC TCGTAAAGGC CCCACTGATA GTCTGTGTAC TGTAACCGAC CTCACTCCTC GTCCGGTCGT GTCACGATGT TCGGACCGTC
324  S  P  R  Q  L  Y  E  H  F  R  G  D  Y  Q  T  H  D  I  G  W  S  E  E  Q  A  S  T  V  L  Q  A  W  Q

1301 CGGCGCTTTG TGCAGCTGGC CCAGGAGGCC CTGCCTGAGA ACGCTTCCCA GCAGATCCAT GCCTTCTCCT CCACCACCCT GGATGACATC CTGCATGCGT
    GCCGCGAAAC ACGTCGACCG GGTCCTCCGG GACGGACTCT TGCGAAGGGT CGTCTAGGTA CGGAAGAGGA GGTGGTGGGA CCTACTGTAG GACGTACGCA
357  R  R  F  V  Q  L  A  Q  E  A  L  P  E  N  A  S  Q  Q  I  H  A  F  S  S  T  T  L  D  D  I  L  H  A  F

1401 TCTCTGAAGT CAGTGCTGCC CGTGTGGTGG GAGGCTATCT GCTCATGCTG GCCTATGCCT GTGTGACCAT GCTGCGGTGG GACTGCGCCC AGTCCCAGGG
    AGAGACTTCA GTCACGACGG GCACACCACC CTCCGATAGA CGAGTACGAC CGGATACGGA CACACTGGTA CGACGCCACC CTGACGCGGG TCAGGGTCCC
391   S  E  V  S  A  A  R  V  V  G  G  Y  L  L  M  L  A  Y  A  C  V  T  M  L  R  W  D  C  A  Q  S  Q  G

1501 TTCCGTGGGC CTTGCCGGGG TACTGCTGGT GGCCCTGGCG GTGGCCTCAG GCCTTGGGCT CTGTGCCCTG CTCGGCATCA CCTTCAATGC TGCCACTACC
    AAGGCACCCG GAACGGCCCC ATGACGACCA CCGGGACCGC CACCGGAGTC CGGAACCCGA GACACGGGAC GAGCCGTAGT GGAAGTTACG ACGGTGATGG
424  S  V  G  L  A  G  V  L  L  V  A  L  A  V  A  S  G  L  G  L  C  A  L  L  G  I  T  F  N  A  A  T  T

1601 CAGGTGCTGC CTTTCTTGGC TCTGGGAATC GGCGTGGATG ACGTATTCCT GCTGGCGCAT GCCTTCACAG AGGCTCTGCC TGGCACCCCT CTCCAGGAGC
    GTCCACGACG GAAAGAACCG AGACCCTTAG CCGCACCTAC TGCATAAGGA CGACCGCGTA CGGAAGTGTC TCCGAGACGG ACCGTGGGGA GAGGTCCTCG
457  Q  V  L  P  F  L  A  L  G  I  G  V  D  D  V  F  L  L  A  H  A  F  T  E  A  L  P  G  T  P  L  Q  E  R

1701 GCATGGGCGA GTGTCTGCAG CGCACGGGCA CCAGTGTCGT ACTCACATCC ATCAACAACA TGGCCGCCTT CCTCATGGCT GCCCTCGTTC CCATCCCTGC
    CGTACCCGCT CACAGACGTC GCGTGCCCGT GGTCACAGCA TGAGTGTAGG TAGTTGTTGT ACCGGCGGAA GGAGTACCGA CGGGAGCAAG GGTAGGGACG
491   M  G  E  C  L  Q  R  T  G  T  S  V  V  L  T  S  I  N  N  M  A  A  F  L  M  A  A  L  V  P  I  P  A
```

FIG. 1B

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```
2701 GCTCATCCAG ACTGGAGACG CCCAGGAGCC TCTGGATTTC AGCCAGCTGA CCACAAGGAA GCTGGTGGAC AGAGAGGGAC TGATTCCACC CGAGCTCTTC
     CGAGTAGGTC TGACCTCTGC GGGTCCTCGG AGACCTAAAG TCGGTCGACT GGTGTTCCTT CGACCACCTG TCTCTCCCTG ACTAAGGTGG GCTCGAGAAG
 824 L  I  Q  T  G  D  A  Q  E  P  L  D  F  S  Q  L  T  T  R  K  L  V  D  R  E  G  L  I  P  P  E  L  F

2801 TACATGGGGC TGACCGTGTG GGTGAGCAGT GACCCCCTGG GTCTGGCAGC CTCACAGGCC AACTTCTACC CCCCACCTCC TGAATGGCTG CACGACAAAT
     ATGTACCCCG ACTGGCACAC CCACTCGTCA CTGGGGGACC CAGACCGTCG GAGTGTCCGG TTGAAGATGG GGGGTGGAGG ACTTACCGAC GTGCTGTTTA
 857 Y  M  G  L  T  V  W  V  S  S  D  P  L  G  L  A  A  S  Q  A  N  F  Y  P  P  P  P  E  W  L  H  D  K  Y

2901 ACGACACCAC GGGGGAGAAC CTTCGCATCC CGCCAGCTCA GCCCTTGGAG TTTGCCCAGT TCCCCTTCCT GCTGCGTGGC CTCCAGAAGA CTGCAGACTT
     TGCTGTGGTG CCCCCTCTTG GAAGCGTAGG GCGGTCGAGT CGGGAACCTC AAACGGGTCA AGGGGAAGGA CGACGCACCG GAGGTCTTCT GACGTCTGAA
  891  D  T  T  G  E  N  L  R  I  P  P  A  Q  P  L  E  F  A  Q  F  P  F  L  L  R  G  L  Q  K  T  A  D  F

3001 TGTGGAGGCC ATCGAGGGGG CCCGGGCAGC ATGCGCAGAG GCCGGCCAGG CTGGGGTGCA CGCCTACCCC AGCGGCTCCC CCTTCCTCTT CTGGGAACAG
     ACACCTCCGG TAGCTCCCCC GGGCCCGTCG TACGCGTCTC CGGCCGGTCC GACCCCACGT GCGGATGGGG TCGCCGAGGG GGAAGGAGAA GACCCTTGTC
 924 V  E  A  I  E  G  A  R  A  A  C  A  E  A  G  Q  A  G  V  H  A  Y  P  S  G  S  P  F  L  F  W  E  Q

3101 TATCTGGGCC TGCGGCGCTG CTTCCTGCTG GCCGTCTGCA TCCTGCTGGT GTGCACTTTC CTCGTCTGTG CTCTGCTGCT CCTCAACCCC TGGACGGCTG
     ATAGACCCGG ACGCCGCGAC GAAGGACGAC CGGCAGACGT AGGACGACCA CACGTGAAAG GAGCAGACAC GAGACGACGA GGAGTTGGGG ACCTGCCGAC
 957 Y  L  G  L  R  R  C  F  L  L  A  V  C  I  L  L  V  C  T  F  L  V  C  A  L  L  L  L  N  P  W  T  A  G

3201 GCCTCATAGT GCTGGTCCTG GCGATGATGA CAGTGGAACT CTTTGGTATC ATGGGTTTCC TGGGCATCAA GCTGAGTGCC ATCCCCGTGG TGATCCTTGT
     CGGAGTATCA CGACCAGGAC CGCTACTACT GTCACCTTGA GAAACCATAG TACCCAAAGG ACCCGTAGTT CGACTCACGG TAGGGGCACC ACTAGGAACA
  991  L  I  V  L  V  L  A  M  M  T  V  E  L  F  G  I  M  G  F  L  G  I  K  L  S  A  I  P  V  V  I  L  V

3301 GGCCTCTGTA GGCATTGGCG TTGAGTTCAC AGTCCACGTG GCTCTGGGCT TCCTGACCAC CCAGGGCAGC CGGAACCTGC GGGCCGCCCA TGCCCTTGAG
     CCGGAGACAT CCGTAACCGC AACTCAAGTG TCAGGTGCAC CGAGACCCGA AGGACTGGTG GGTCCCGTCG GCCTTGGACG CCCGGCGGGT ACGGGAACTC
 1024 A  S  V  G  I  G  V  E  F  T  V  H  V  A  L  G  F  L  T  T  Q  G  S  R  N  L  R  A  A  H  A  L  E

3401 CACACATTTG CCCCCGTGAC CGATGGGGCC ATCTCCACAT TGCTGGGTCT GCTCATGCTT GCTGGTTCCC ACTTTGACTT CATTGTAAGG TACTTCTTTG
     GTGTGTAAAC GGGGGCACTG GCTACCCCGG TAGAGGTGTA ACGACCCAGA CGAGTACGAA CGACCAAGGG TGAAACTGAA GTAACATTCC ATGAAGAAAC
 1057 H  T  F  A  P  V  T  D  G  A  I  S  T  L  L  G  L  L  M  L  A  G  S  H  F  D  F  I  V  R  Y  F  F  A

3501 CGGCGCTGAC AGTGCTCACG CTCCTGGGCC TCCTCCATGG ACTCGTGCTG CTGCCTGTGC TGCTGTCCAT CCTGGGCCCG CCGCCAGAGG TGATACAGAT
     GCCGCGACTG TCACGAGTGC GAGGACCCGG AGGAGGTACC TGAGCACGAC GACGGACACG ACGACAGGTA GGACCCGGGC GGCGGTCTCC ACTATGTCTA
 1091  A  L  T  V  L  T  L  L  G  L  L  H  G  L  V  L  L  P  V  L  L  S  I  L  G  P  P  P  E  V  I  Q  M
```

FIG. 1D

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```
3601 GTACAAGGAA AGCCCAGAGA TCCTGAGTCC ACCAGCTCCA CAGGGAGGCG GGCTTAGGTG GGGGGCATCC TCCTCCCTGC CCCAGAGCTT TGCCAGAGTG
     CATGTTCCTT TCGGGTCTCT AGGACTCAGG TGGTCGAGGT GTCCCTCCGC CCGAATCCAC CCCCCGTAGG AGGAGGGACG GGGTCTCGAA ACGGTCTCAC
1124   Y  K  E  S  P  E  I  L  S  P  P  A  P  Q  G  G  G  L  R  W  G  A  S  S  S  L  P  Q  S  F  A  R  V

3701 ACTACCTCCA TGACCGTGGC CATCCACCCA CCCCCCCTGC CTGGTGCCTA CATCCATCCA GCCCCTGATG AGCCCCCTTG GTCCCCTGCT GCCACTAGCT
     TGATGGAGGT ACTGGCACCG GTAGGTGGGT GGGGGGGACG GACCACGGAT GTAGGTAGGT CGGGGACTAC TCGGGGGAAC CAGGGGACGA CGGTGATCGA
1157 T  T  S  M  T  V  A  I  H  P  P  P  L  P  G  A  Y  I  H  P  A  P  D  E  P  P  W  S  P  A  A  T  S  S

3801 CTGGCAACCT CAGTTCCAGG GGACCAGGTC CAGCCACTGG GTGAAAGAGC AGCTGAAGCA CAGAGACCAT GTGTGGGGCG TGTGGGGTCA CTGGGAAGCA
     GACCGTTGGA GTCAAGGTCC CCTGGTCCAG GTCGGTGACC CACTTTCTCG TCGACTTCGT GTCTCTGGTA CACACCCCGC ACACCCCAGT GACCCTTCGT
1191   G  N  L  S  S  R  G  P  G  P  A  T  G  O
                                          ~~1203~~

3901 CTGGGTCTGG TGTTAGACGC AGGACGGACC CCTGGAGGGC CCTGCTGCTG CTGCATCCCC TCTCCCGACC CAGCTGTCAT GGGCCTCCCT GATATCGAAT
     GACCCAGACC ACAATCTGCG TCCTGCCTGG GGACCTCCCG GGACGACGAC GACGTAGGGG AGAGGGCTGG GTCGACAGTA CCCGGAGGGA CTATAGCTTA
                          ~~A to C (silent)~~                    ~~pRK follows, this is the 5prime end of vector~~

4001 TCAATCGATA GAACCGAGGT GCAGTTGGAC
     AGTTAGCTAT CTTGGCTCCA CGTCAACCTG
```

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FIG. 1E

(SEQ ID NO: 3)

```
                    30        40        50        60        70
905531      GCTGGGGTGCACGCCTACCNCAGCGGNTCCCCCTTCCTCTTCTGGGAACA
              ::: ::  :   ******* ***** ******************** **
hpatched    CTGGGGCTGTCCAGTTACCCCAACGGCTACCCCTTCCTCTTCTGGGAGCA
(SEQ ID NO: 4)
          3010      3020      3030      3040      3050

                   80        90       100       110       120
905531      GTATCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGG
            ***  * ***** ** * ***  * ******  * ** ** *  ** ***
hpatched    GTACATCGGCCTCCGCCACTGGCTGCTGCTGTTCATCAGCGTGGTGTTGG
          3060      3070      3080      3090      3100

                  130       140       150       160       170
905531      TGTGCACTTTCCTCGTCTGTGCTCTGCTGCTCCTNAACCCCTGGACGGCT
            ***** ******** ** *** *  * ** ****************
hpatched    CCTGCACATTCCTCGTGTGCGCTGTCTTCCTTCTGAACCCCTGGACGGCC
          3110      3120      3130      3140      3150

                  180       190       200       210       220
905531      GGCCTNATAGTGCTGGTCCTGGCGATGATGACAGTGGAACTCTTTGGTAT
            **  **** *** ********** ******* ** ** ** ** ** **
hpatched    GGGATCATTGTGATGGTCCTGGCGCTGATGACGGTCGAGCTGTTCGGCAT
          3160      3170      3180      3190      3200

                  230       240       250
905531      CATGGGTTTNCTGGGCATCAAGCTGAGT
             *****  ** * ** ******** ***
hpatched    GATGGGCCTCATCGGAATCAAGCTCAGT
          3210      3220      3230
```

```
                   80        90       100       110       120
905531      TCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGGTGT
             :::   :::      * ** *  ** *****   ****   * ** ****
hpatched    GCTGCTGCTGTTCATCAGCGTGGTGTTGGCC---TGCACATTCCTCGTGT
                  3090      3100      3110          3120

                  130       140       150
905531      GCACTTTCCTCGTCTGTGCTCTGCTGCT
            ** ** ** ** *       :    :
hpatched    GCGCTGTCTTCCTTCTGAACCCCTGGAC
          3130      3140      3150
```

FIG. 2A

```
                30          40          50          60          70
(SEQ ID NO:5) 1326258    GCTGGGGTGCACGCCTACCCCAGCGGCTCCCCCTTCCTCTTCTGGGAACA
                  ::: ::  :   ******* ***** ******************** **
hpatched      CTGGGGCTGTCCAGTTACCCCAACGGCTACCCCTTCCTCTTCTGGGAGCA
           3010        3020        3030        3040        3050

                80          90         100         110         120
1326258       GTATCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGG
              ***  * ***** ** * ***  * ******  * ** ** *  ** ***
hpatched      GTACATCGGCCTCCGCCACTGGCTGCTGCTGTTCATCAGCGTGGTGTTGG
           3060        3070        3080        3090        3100

              130         140         150
1326258       TGTGCACTTTCCTCNTCTGTGCTCT
              ***** ******** ** *** *
hpatched      CCTGCACATTCCTCGTGTGCGCTGT
           3110        3120        3130
```

```
                   90          100         110         120         130
1326258       TCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGGTGT
               :::   :::      * ** *  ** *****   ****   * ** ****
hpatched      GCTGCTGCTGTTCATCAGCGTGGTGTTGGCC---TGCACATTCCTCGTGT
                 3090        3100        3110          3120

                  140         150
1326258       GCACTTTCCTCNTCTGTGCTCT
              ** **. ** ****       :
hpatched      GCGCTGTCTTCCTTCTGAACCC
           3130        3140
```

```
                        10          20          30          40          50
1326258          CCGGGCAGCATGCGCAGAGGCCGGCCAGGCTGGGGTGCACGCCTACCCCA
                 ****** *****    ** ** * *** ******* *      :
(SEQ ID NO:6) hpatched.RC  CCGGGCGGCATG--GCGAAGCGGACCACGCTGGGGGGTGGCTCAGGGGAG
                      710         720         730         740         750
```

FIG. 2B

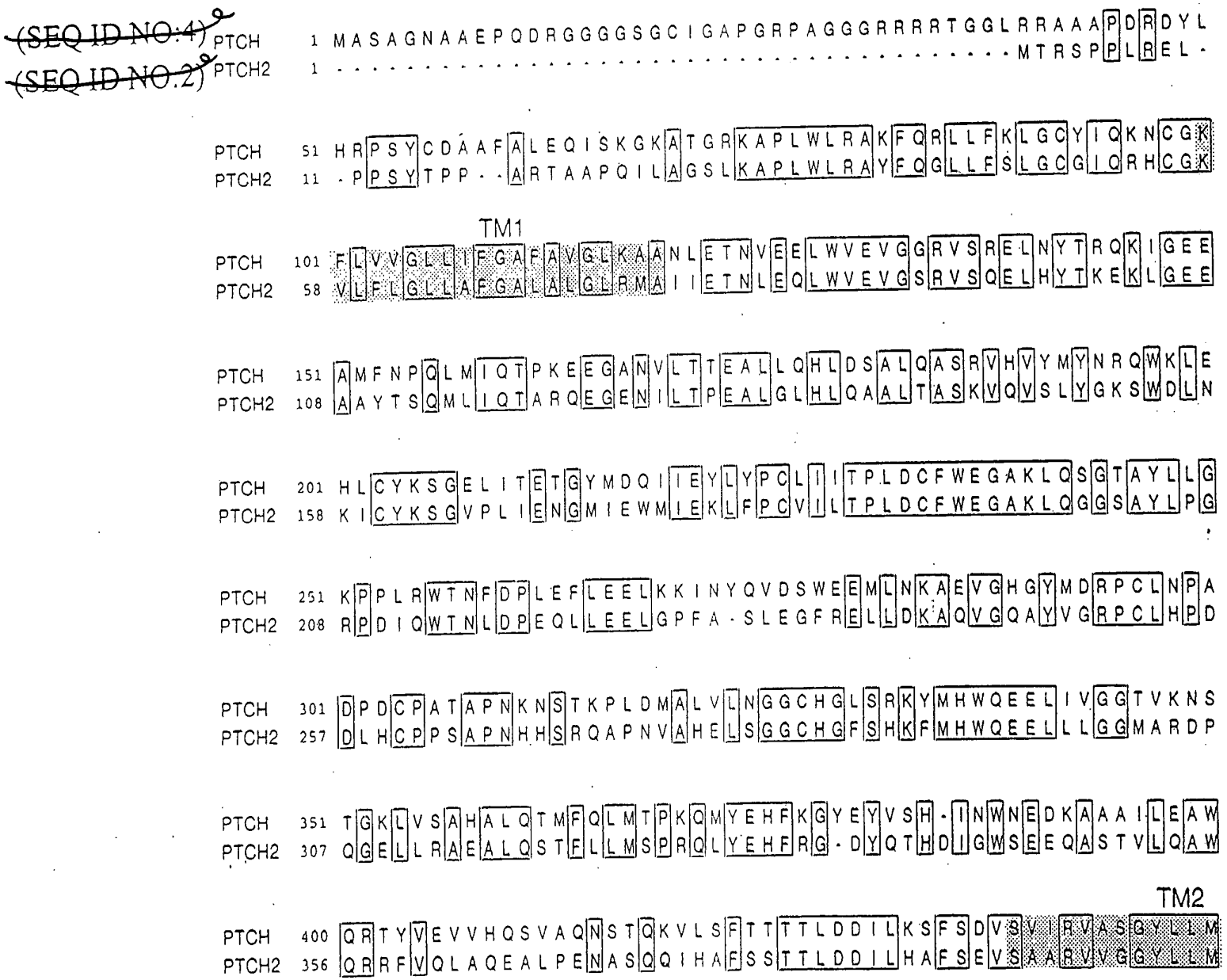

FIG. 3A

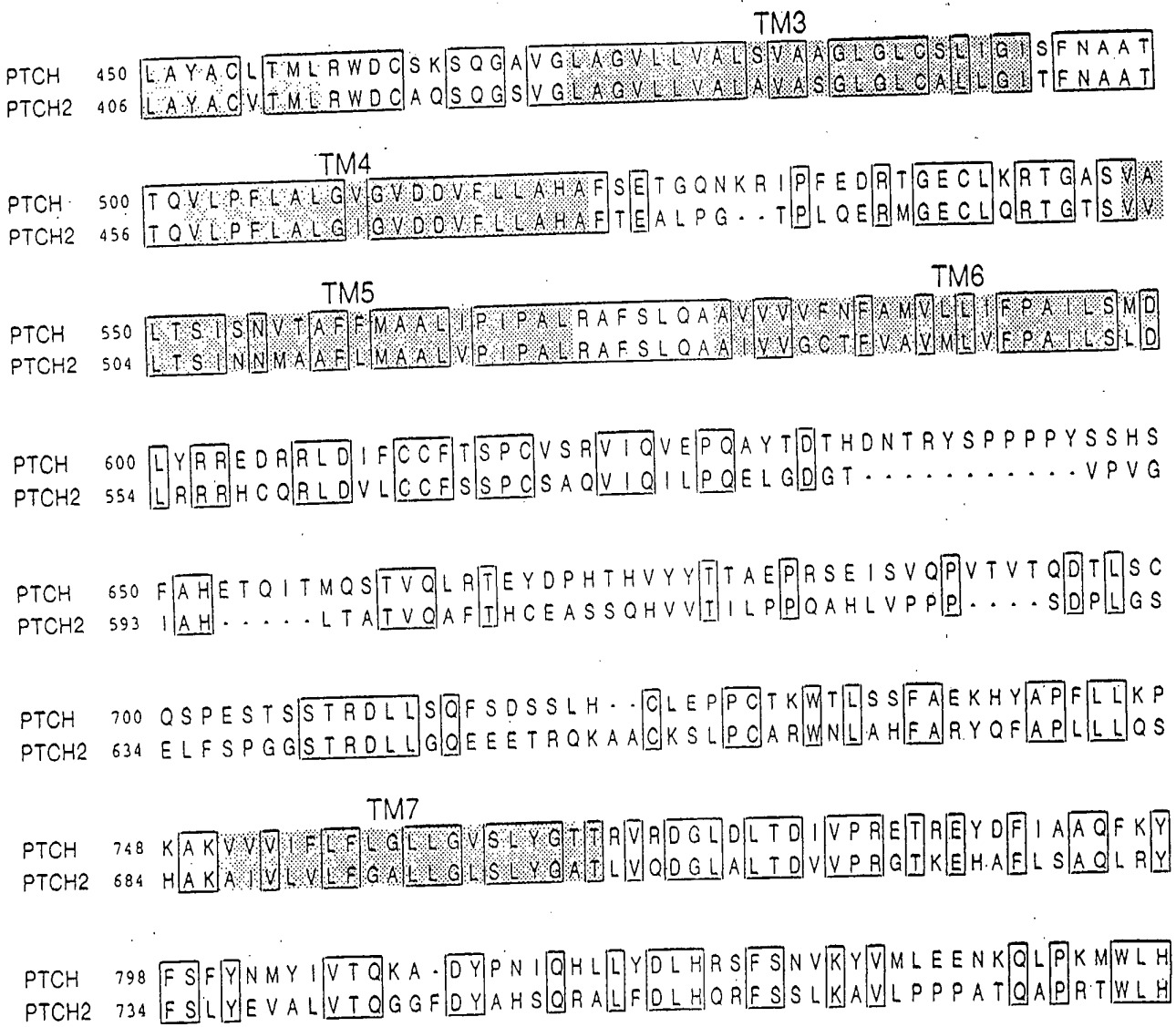
TM3
PTCH 450 LAYACLTMLRWDCSKSQGAVGLAGVLLVALSVAAGLGLCSLIGISFNAAT
PTCH2 406 LAYACVTMLRWDCAQSQGSVGLAGVLLVALAVASGLQLCALLGITFNAAT
TM4
PTCH 500 TQVLPFLALGVGVDDVFLLAHAFSETGQNKRIPFEDRTGECLKRTGASYA
PTCH2 456 TQVLPFLALGIGVDDVFLLAHAFTEALPG--TPLQERMGECLQRTGTSVV
TM5
TM6
PTCH 550 LTSISNVTAFFMAALIPIPALRAFSLQAAVVVFNFAMVLLIFPAILSMD
PTCH2 504 LTSINNMAAFLMAALVPIPALRAFSLQAAIVVGCTFVAVMLVFPAILSLD
PTCH 600 LYRREDRRLDIFCCFTSPCVSRVIQVEPQAYTDTHDNTRYSPPPPYSSHS
PTCH2 554 LRRRHCQRLDVLCCFSSPCSAQVIQILPQELGDGT----------VPVG
PTCH 650 FAHETQITMQSTVQLRTEYDPHTHVYYTTAEPRSEISVQPVTVTQDTLSC
PTCH2 593 IAH----LTATVQAFTHCEASSQHVVTILPPQAHLVPPP----SDPLGS
PTCH 700 QSPESTSSTRDLLSQFSDSSLH--CLEPPCTKWTLSSFAEKHYAPFLLKP
PTCH2 634 ELFSPGGSTRDLLGQEEETRQKAACKSLPCARWNLAHFARYQFAPLLLQS
TM7
PTCH 748 KAKVVVIFLFLGLLGVSLYGTTRVRDGLDLTDIVPRETREYDFIAAQFKY
PTCH2 684 HAKAIVLVLFGALLGLSLYGATLVQDGLALTDVVPRGTKEHAFLSAQLRY
PTCH 798 FSFYNMYIVTQKA-DYPNIQHLLYDLHRSFSNVKYVMLEENKQLPKMWLH
PTCH2 734 FSLYEVALVTQGGFDYAHSQRALFDLHQRFSSLKAVLPPPATQAPRTWLH

FIG. 3B

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FIG. 3C

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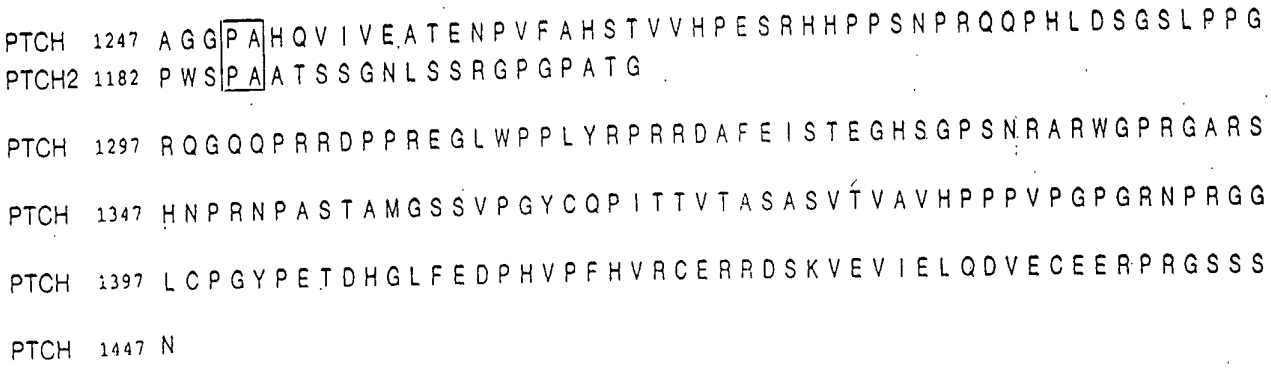
PTCH 1247 AGGPAHQVIVEATENPVFAHSTVVHPESRHHPPSNPRQQPHLDSGSLPPG
PTCH2 1182 PWSPAATSSGNLSSRGPGPATG
PTCH 1297 RQGQQPRRDPPREGLWPPLYRPRRDAFEISTEGHSGPSNRARWGPRGARS
PTCH 1347 HNPRNPASTAMGSSVPGYCQPITTVTASASVTVAVHPPPVPGPGRNPRGG
PTCH 1397 LCPGYPETDHGLFEDPHVPFHVRCERRDSKVEVIELQDVECEERPRGSSS
PTCH 1447 N

FIG. 3D

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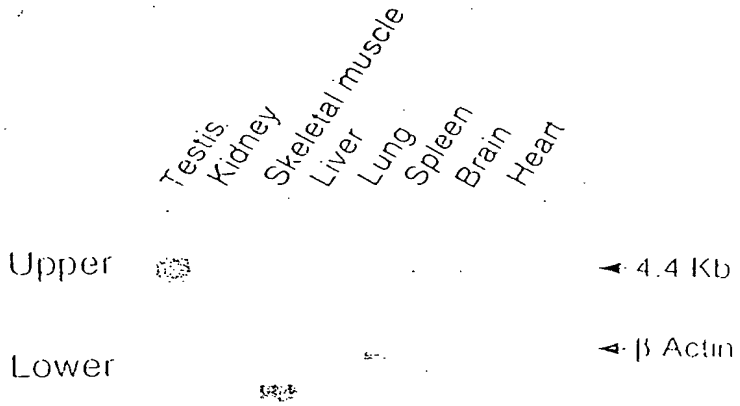

FIG. 4

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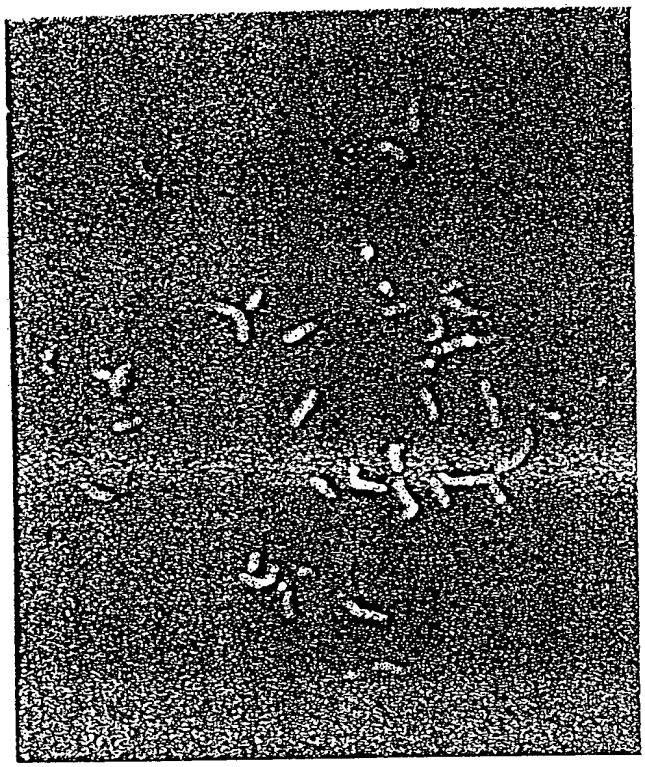

FIG. 5

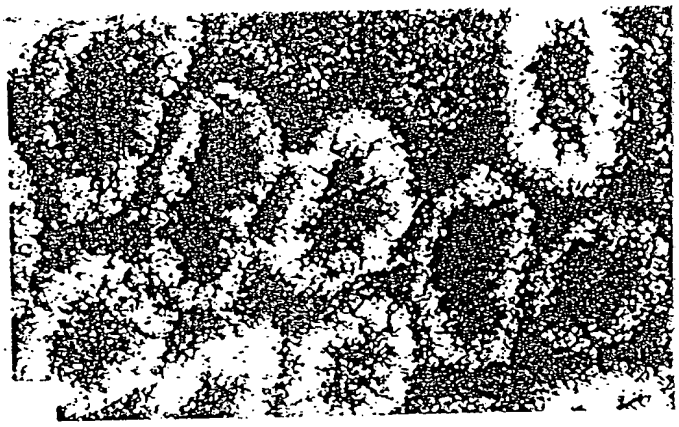

FIG. 6C

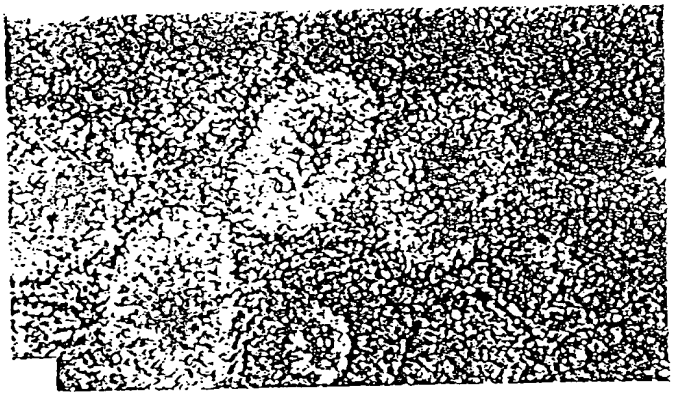

FIG. 6B

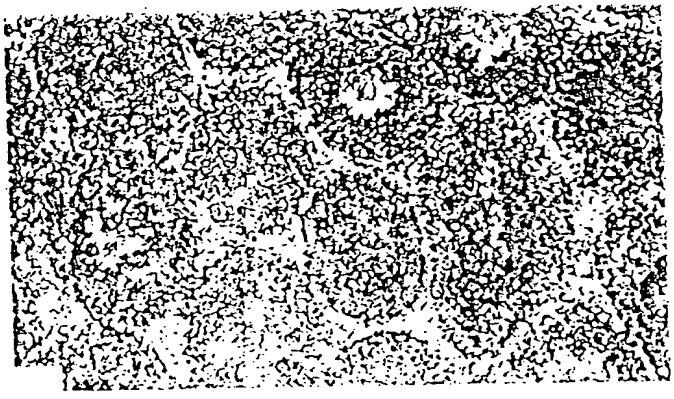

FIG. 6A

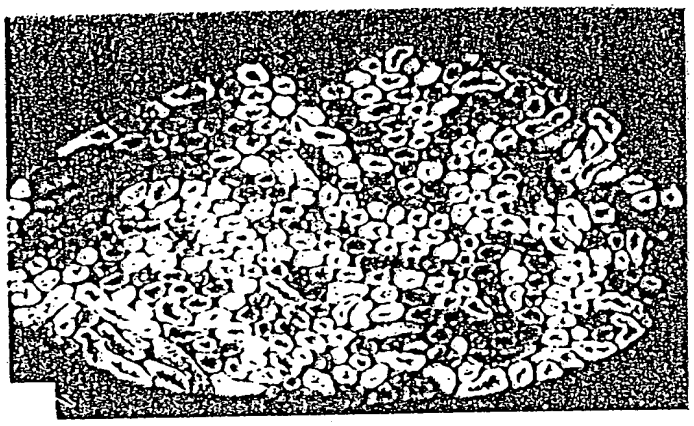

FIG. 6F

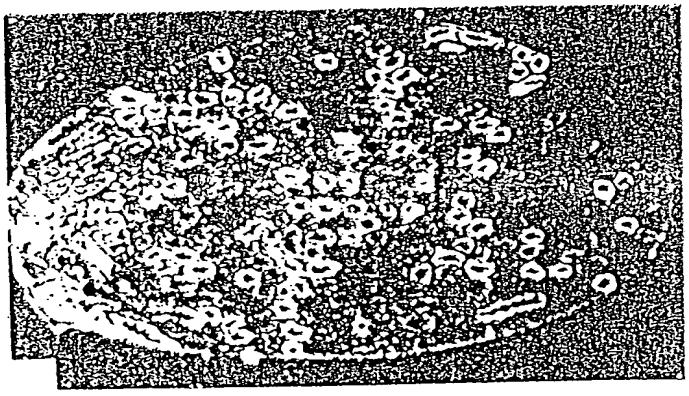

FIG. 6E

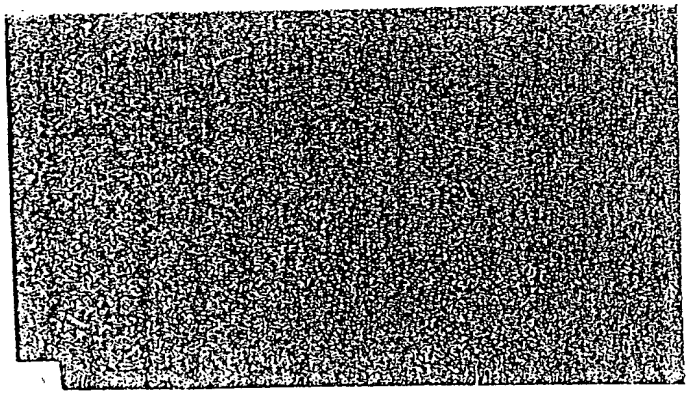

FIG. 6D

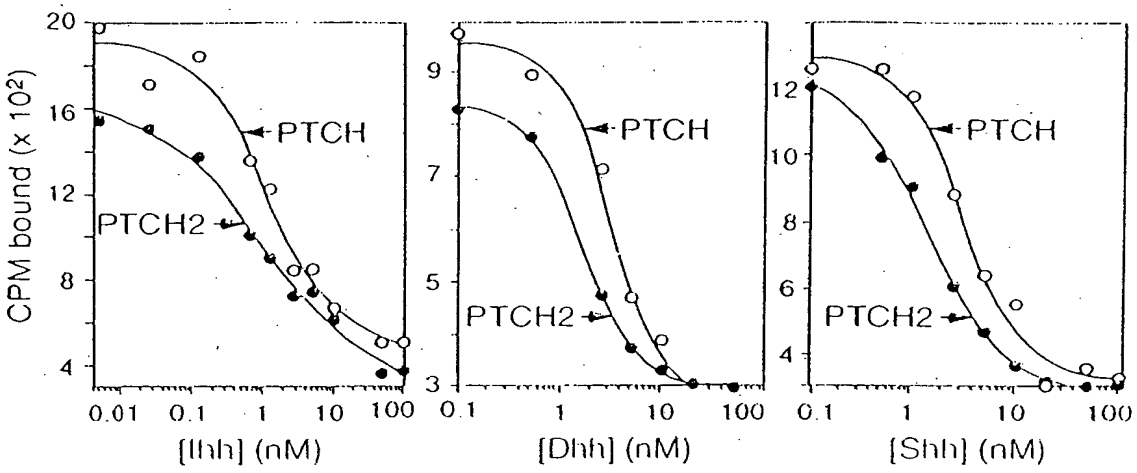
CPM bound (x 10²)
PTCH
PTCH2
[Ihh] (nM)
[Dhh] (nM)
[Shh] (nM)

FIG. 7A

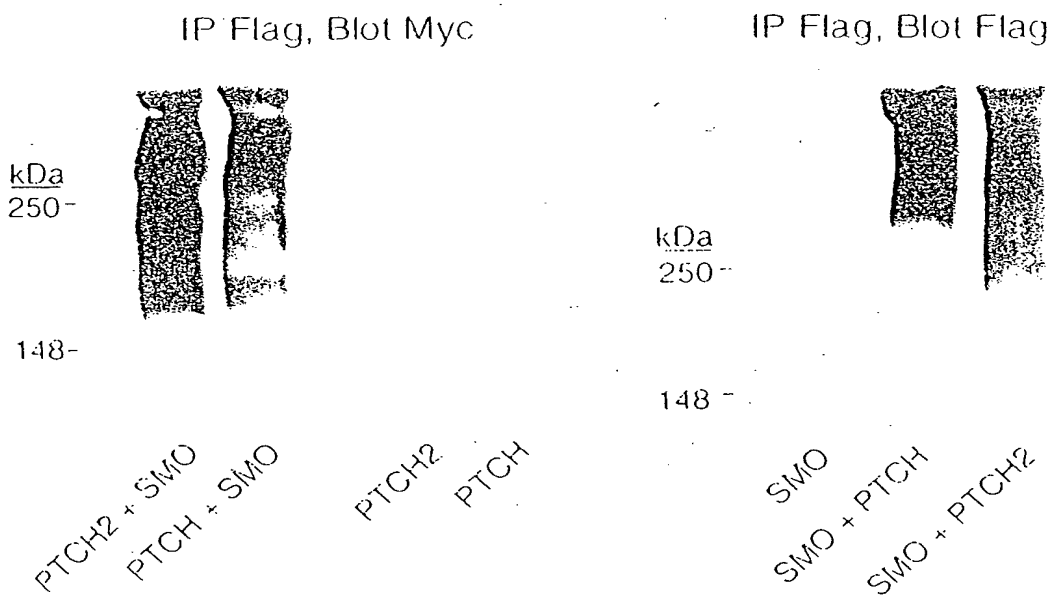
IP Flag, Blot Myc
IP Flag, Blot Flag
kDa
250
148
PTCH2 + SMO
PTCH + SMO
PTCH2
PTCH
SMO
SMO + PTCH
SMO + PTCH2

FIG. 7B

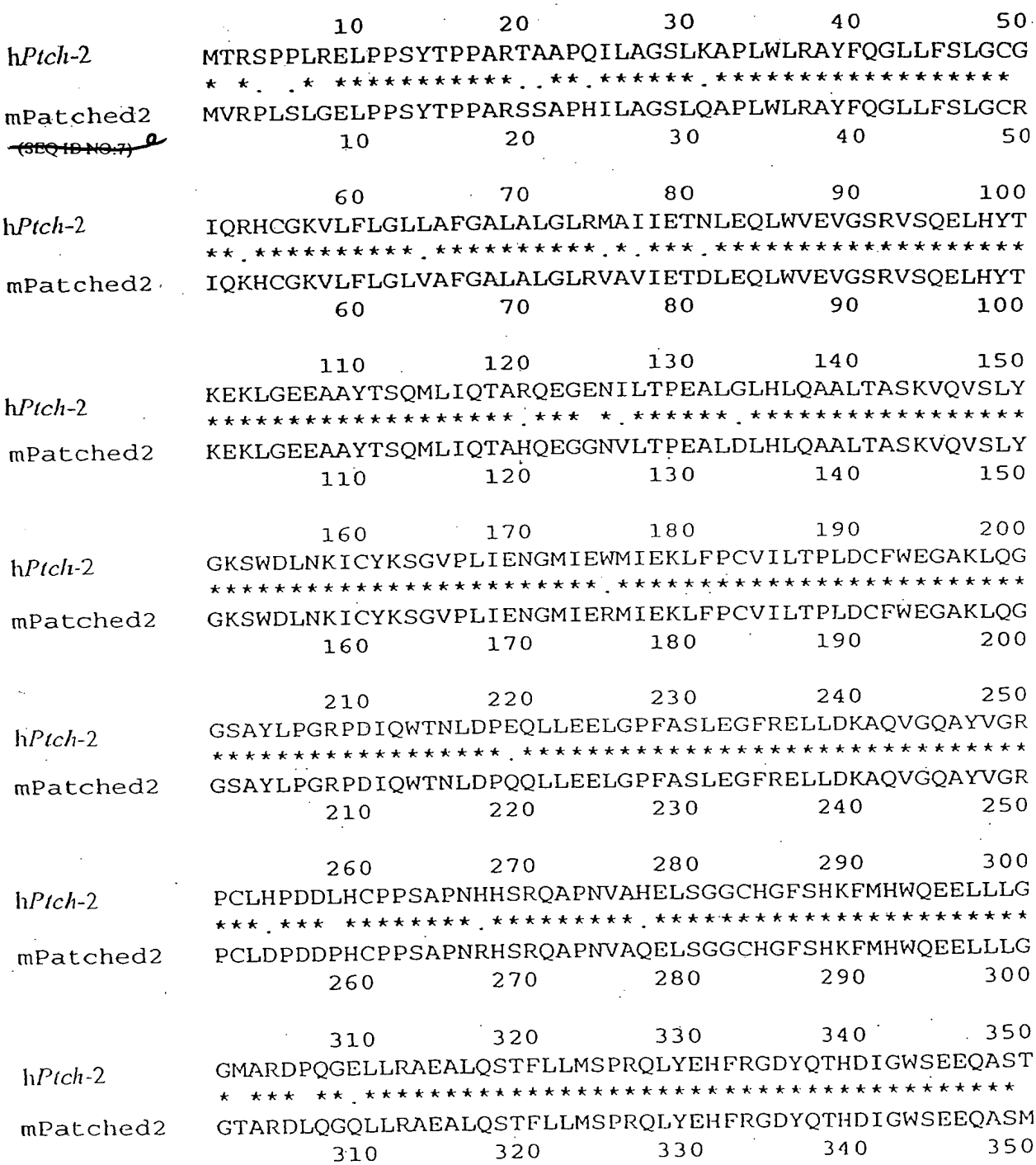
10 20 30 40 50
hPtch-2 MTRSPPLRELPPSYTPPARTAAPQILAGSLKAPLWLRAYFQGLLFSLGCG
mPatched2 MVRPLSLGELPPSYTPPARSSAPHILAGSLQAPLWLRAYFQGLLFSLGCR
10 20 30 40 50
60 70 80 90 100
hPtch-2 IQRHCGKVLFLGLLAFGALALGLRMAIIETNLEQLWVEVGSRVSQELHYT
mPatched2 IQKHCGKVLFLGLVAFGALALGLRVAVIETDLEQLWVEVGSRVSQELHYT
60 70 80 90 100
110 120 130 140 150
hPtch-2 KEKLGEEAAYTSQMLIQTARQEGENILTPEALGLHLQAALTASKVQVSLY
mPatched2 KEKLGEEAAYTSQMLIQTAHQEGGNVLTPEALDLHLQAALTASKVQVSLY
110 120 130 140 150
160 170 180 190 200
hPtch-2 GKSWDLNKICYKSGVPLIENGMIEWMIEKLFPCVILTPLDCFWEGAKLQG
mPatched2 GKSWDLNKICYKSGVPLIENGMIERMIEKLFPCVILTPLDCFWEGAKLQG
160 170 180 190 200
210 220 230 240 250
hPtch-2 GSAYLPGRPDIQWTNLDPEQLLEELGPFASLEGFRELLDKAQVGQAYVGR
mPatched2 GSAYLPGRPDIQWTNLDPQQLLEELGPFASLEGFRELLDKAQVGQAYVGR
210 220 230 240 250
260 270 280 290 300
hPtch-2 PCLHPDDLHCPPSAPNHHSRQAPNVAHELSGGCHGFSHKFMHWQEELLLG
mPatched2 PCLDPDDPHCPPSAPNRHSRQAPNVAQELSGGCHGFSHKFMHWQEELLLG
260 270 280 290 300
310 320 330 340 350
hPtch-2 GMARDPQGELLRAEALQSTFLLMSPRQLYEHFRGDYQTHDIGWSEEQAST
mPatched2 GTARDLQGQLLRAEALQSTFLLMSPRQLYEHFRGDYQTHDIGWSEEQASM
310 320 330 340 350

FIG. 8A

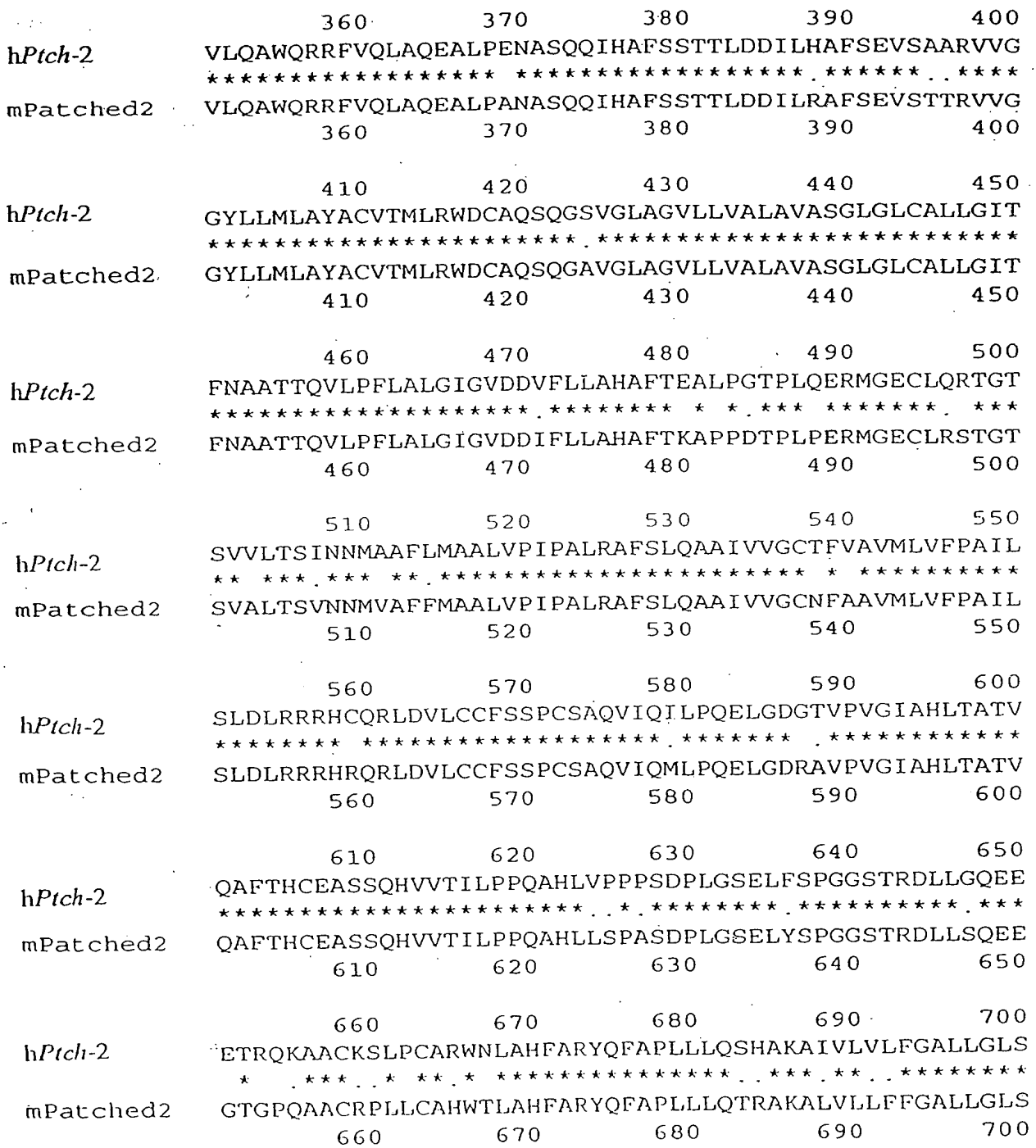
360 370 380 390 400
hPtch-2 VLQAWQRRFVQLAQEALPENASQQIHAFSSTTLDDILHAFSEVSAARVVG
mPatched2 VLQAWQRRFVQLAQEALPANASQQIHAFSSTTLDDILRAFSEVSTTRVVG
360 370 380 390 400
410 420 430 440 450
hPtch-2 GYLLMLAYACVTMLRWDCAQSQGSVGLAGVLLVALAVASGLGLCALLGIT
mPatched2 GYLLMLAYACVTMLRWDCAQSQGAVGLAGVLLVALAVASGLGLCALLGIT
410 420 430 440 450
460 470 480 490 500
hPtch-2 FNAATTQVLPFLALGIGVDDVFLLAHAFTEALPGTPLQERMGECLQRTGT
mPatched2 FNAATTQVLPFLALGIGVDDIFLLAHAFTKAPPDTPLPERMGECLRSTGT
460 470 480 490 500
510 520 530 540 550
hPtch-2 SVVLTSINNMAAFLMAALVPIPALRAFSLQAAIVVGCTFVAVMLVFPAIL
mPatched2 SVALTSVNNMVAFFMAALVPIPALRAFSLQAAIVVGCNFAAVMLVFPAIL
510 520 530 540 550
560 570 580 590 600
hPtch-2 SLDLRRRHCQRLDVLCCFSSPCSAQVIQILPQELGDGTVPVGIAHLTATV
mPatched2 SLDLRRRHRQRLDVLCCFSSPCSAQVIQMLPQELGDRAVPVGIAHLTATV
560 570 580 590 600
610 620 630 640 650
hPtch-2 QAFTHCEASSQHVVTILPPQAHLVPPPSDPLGSELFSPGGSTRDLLGQEE
mPatched2 QAFTHCEASSQHVVTILPPQAHLLSPASDPLGSELYSPGGSTRDLLSQEE
610 620 630 640 650
660 670 680 690 700
hPtch-2 ETRQKAACKSLPCARWNLAHFARYQFAPLLLQSHAKAIVLVLFGALLGLS
mPatched2 GTGPQAACRPLLCAHWTLAHFARYQFAPLLLQTRAKALVLLFFGALLGLS
660 670 680 690 700

FIG. 8B

```
                710         720         730         740         750
hPtch-2         LYGATLVQDGLALTDVVPRGTKEHAFLSAQLRYFSLYEVALVTQGGFDYA
                **************************************************
mPatched2       LYGATLVQDGLALTDVVPRGTKEHAFLSAQLRYFSLYEVALVTQGGFDYA
                710         720         730         740         750

                760         770         780         790         800
hPtch-2         HSQRALFDLHQRFSSLKAVLPPPATQAPRTWLHYYRNWLQGIQAAFDQDW
                ********************************** **********
mPatched2       HSQRALFDLHQRFSSLKAVLPPPATQAPRTWLHYYRSWLQGIQAAFDQDW
                760         770         780         790         800

                810         820         830         840         850
hPtch-2         ASGRITRHSYRNGSEDGALAYKLLIQTGDAQEPLDFSQLTTRKLVDREGL
                ****** ********************* ***************** ***
mPatched2       ASGRITCHSYRNGSEDGALAYKLLIQTGNAQEPLDFSQLTTRKLVDKEGL
                810         820         830         840         850

                860         870         880         890         900
hPtch-2         IPPELFYMGLTVWVSSDPLGLAASQANFYPPPPEWLHDKYDTTGENLRIP
                **************************************************
mPatched2       IPPELFYMGLTVWVSSDPLGLAASQANFYPPPPEWLHDKYDTTGENLRIP
                860         870         880         890         900

                910         920         930         940         950
hPtch-2         PAQPLEFAQFPFLLRGLQKTADFVEAIEGARAACAEAGQAGVHAYPSGSP
                ************ ****************** ***************
mPatched2       AAQPLEFAQFPFLLHGLQKTADFVEAIEGARAACTEAGQAGVHAYPSGSP
                910         920         930         940         950

                960         970         980         990        1000
hPtch-2         FLFWEQYLGLRRCFLLAVCILLVCTFLVCALLLLNPWTAGLIVLVLAMMT
                ********************************** ***************
mPatched2       FLFWEQYLGLRRCFLLAVCILLVCTFLVCALLLLSPWTAGLIVLVLAMMT
                960         970         980         990        1000

                1010        1020        1030        1040        1050
hPtch-2         VELFGIMGFLGIKLSAIPVVILVASVGIGVEFTVHVALGFLTTQGSRNLR
                ************************ **************** ******
mPatched2       VELFGIMGFLGIKLSAIPVVILVASIGIGVEFTVHVALGFLTSHGSRNLR
                1010        1020        1030        1040        1050
```

FIG. 8C

```
                1060       1070       1080       1090       1100
hPtch-2         AAHALEHTFAPVTDGAISTLLGLLMLAGSHFDFIVRYFFAALTVLTLLGL
                ** ***.*********.***********.****.****  *********
mPatched2       AASALEQTFAPVTDGAVSTLLGLLMLAGSNFDFIIRYFFVVLTVLTLLGL
                1060       1070       1080       1090       1100

                1110       1120       1130       1140       1150
hPtch-2         LHGLVLLPVLLSILGPPPEVIQMYKESPEILSPPAPQGGGLRWGASSSLP
                ****.*************.*.*.*****. *...*** *****. ...**
mPatched2       LHGLLLLPVLLSILGPPPQVVQVYKESPQTLNSAAPQRGGLRWDRPPTLP
                1110       1120       1130       1140       1150

                1160       1170       1180       1190       1200
hPtch-2         QSFARVTTSMTVAIHPPPLPGAYIHPAPDEPPWSPAATSSGNLSSRGPGP
                ************.*********.***..**
mPatched2       QSFARVTTSMTVALHPPPLPGAYVHPASEEPT
                1160       1170       1180

hPtch-2         ATG
```

FIG. 8D

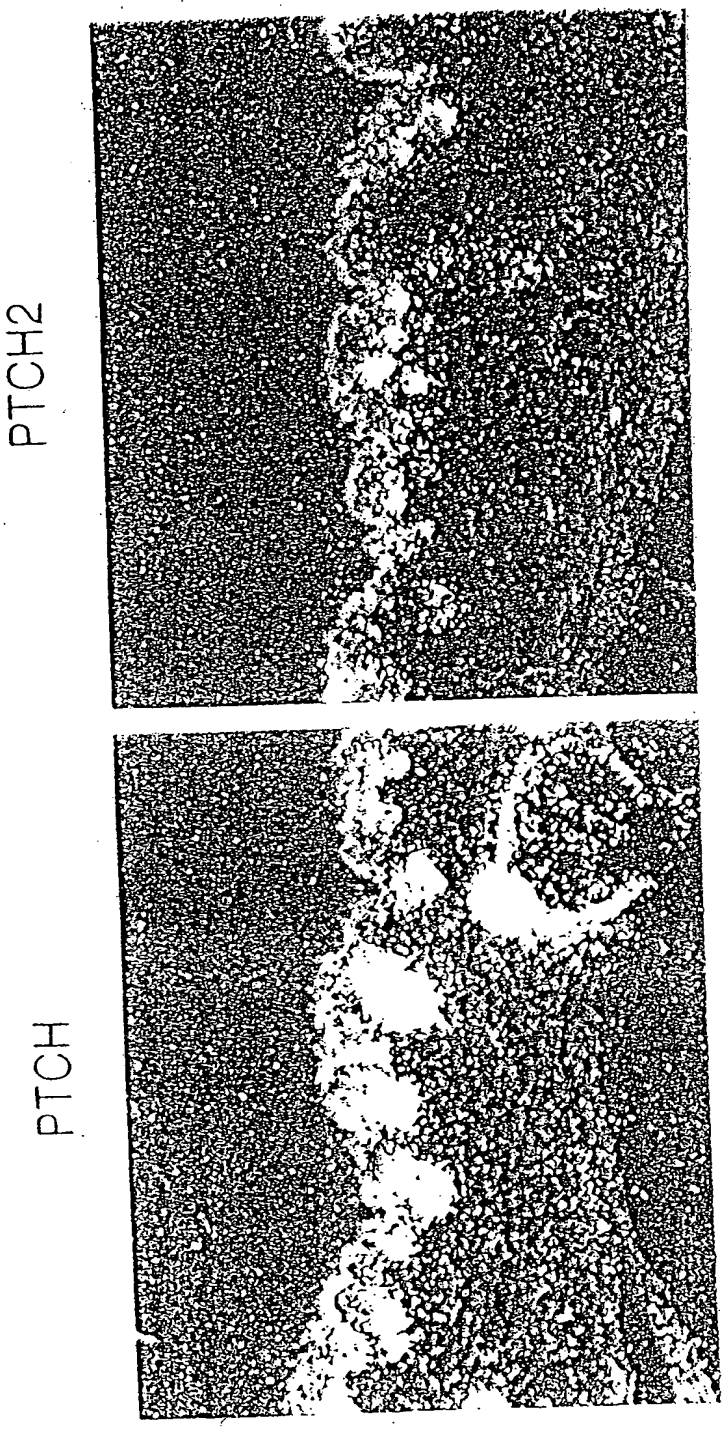

FIG. 9

~~> Consensus Sequence of human patched 2 cDNA clone~~
~~> length: 4004 bp~~

~~(SEQ ID NO:8)~~

```
1 CCCACGCGTC CGGGAGAAGC TGGGGGAGGA GGCTGCATAC ACCTCTCAGA TGCTGATACA GACCGCACGC CAGGAGGGAG AGAACATCCT CACACCCGAA
  GGGTGCGCAG GCCCTCTTCG ACCCCCTCCT CCGACGTATG TGGAGAGTCT ACGACTATGT CTGGCGTGCG GTCCTCCCTC TCTTGTAGGA GTGTGGGCTT

101 GCACTTGGCC TCCACCTCCA GGCAGCCCTC ACTGCCAGTA AAGTCCAAGT ATCACTCTAT GGGAAGTCCT GGGATTTGAA CAAAATCTGC TACAAGTCAG
    CGTGAACCGG AGGTGGAGGT CCGTCGGGAG TGACGGTCAT TTCAGGTTCA TAGTGAGATA CCCTTCAGGA CCCTAAACTT GTTTTAGACG ATGTTCAGTC

201 GAGTTCCCCT TATTGAAAAT GGAATGATTG AGCGGATGAT TGAGAAGCTG TTTCCGTGCG TGATCCTCAC CCCCCTCGAC TGCTTCTGGG AGGGAGCCAA
    CTCAAGGGGA ATAACTTTTA CCTTACTAAC TCGCCTACTA ACTCTTCGAC AAAGGCACGC ACTAGGAGTG GGGGGAGCTG ACGAAGACCC TCCCTCGGTT

301 ACTCCAAGGG GGCTCCGCCT ACCTGCCGCT CCCAATGTGG CTCACGAGCT GAGTGGGGGC TGCCATGGCT TCTCCCACAA ATTCATGCAC TGGCAGGAGG
    TGAGGTTCCC CCGAGGCGGA TGGACGGCGA GGGTTACACC GAGTGCTCGA CTCACCCCCG ACGGTACCGA AGAGGGTGTT TAAGTACGTG ACCGTCCTCC

401 AATTGCTGCT GGGAGGCATG GCCAGAGACC CCCAAGGAGA GCTGCTGAGG GCAGAGGCCC TGCAGAGCAC CTTCTTGCTG ATGAGTCCCC GCCAGCTGTA
    TTAACGACGA CCCTCCGTAC CGGTCTCTGG GGGTTCCTCT CGACGACTCC CGTCTCCGGG ACGTCTCGTG GAAGAACGAC TACTCAGGGG CGGTCGACAT

501 CGAGCATTTC CGGGGTGACT ATCAGACACA TGACATTGGC TGGAGTGAGG AGCAGGCCAG CACAGTGCTA CAAGCCTGGC AGCGGCGCTT TGTGCAGGTC
    GCTCGTAAAG GCCCCACTGA TAGTCTGTGT ACTGTAACCG ACCTCACTCC TCGTCCGGTC GTGTCACGAT GTTCGGACCG TCGCCGCGAA ACACGTCCAG

601 GGTATGGACA AGGACAGGGG GGTGCCCTGA GGCCATTCCC TCCTCCTGCC CCCTCCTATC CACCCTGTTT CTCCAGCTGG CCCAGGAGGC CCTGCCTGAG
    CCATACCTGT TCCTGTCCCC CCACGGGACT CCGGTAAGGG AGGAGGACGG GGGAGGATAG GTGGGACAAA GAGGTCGACC GGGTCCTCCG GGACGGACTC

701 AACGCTTCCC AGCAGATCCA TGCCTTCTCC TCCACCACCC TGGATGACAT CCTGCATGCG TTCTCTGAAG TCAGTGCTGC CCGTGTGGTG GGAGGCTATC
    TTGCGAAGGG TCGTCTAGGT ACGGAAGAGG AGGTGGTGGG ACCTACTGTA GGACGTACGC AAGAGACTTC AGTCACGACG GGCACACCAC CCTCCGATAG

801 TGCTCATGGT GGGTCTTGCA CCTGGCACCT TGCCCCCACC CCACCTCCAA CCAGTGCCCA CCCTGGGGAG CCCCTGAGAC TGCCCTTTCC CCCCACAGCT
    ACGAGTACCA CCCAGAACGT GGACCGTGGA ACGGGGGTGG GGTGGAGGTT GGTCACGGGT GGGACCCCTC GGGGACTCTG ACGGGAAAGG GGGGTGTCGA
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FIG. 10A

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901 GGCCTATGCC TGTGTGACCA TGCTGCGGTG GGACTGCGCC CAGTCCCAGG GTTCCGTGGG CCTTGCCGGG GTACTGCTGG TGGCCCTGGC GGTGGCCTCA
    CCGGATACGG ACACACTGGT ACGACGCCAC CCTGACGCGG GTCAGGGTCC CAAGGCACCC GGAACGGCCC CATGACGACC ACCGGGACCG CCACCGGAGT

1001 GGCCTTGGGC TCTGTGCCCT GCTCGGCATC ACCTTCAATG CTGCCACTAC CCAGGTACGC CAGGACTGCA GGGCAGACTC AGTGCCAGTC ACCAGGCTTC
     CCGGAACCCG AGACACGGGA CGAGCCGTAG TGGAAGTTAC GACGGTGATG GGTCCATGCG GTCCTGACGT CCCGTCTGAG TCACGGTCAG TGGTCCGAAG

1101 ACGGGTCCTC AGCTGCCCGC TCCTCTGCCC CTCCAGGTGC TGCCCTTCTT GACTCTGGGA ATCGGCGTGG ATGACGTATT CCTGCTGGCG CATGCCTTCA
     TGCCCAGGAG TCGACGGGCG AGGAGACGGG GAGGTCCACG ACGGGAAGAA CTGAGACCCT TAGCCGCACC TACTGCATAA GGACGACCGC GTACGGAAGT

1201 CAGAGGCTCT GCCTGGCACC CCTCTCCAGG TGGGGCCTTG TCCCCCAGGG CTCATCTGAG GCAGCTCAGC TTACTGGTTA AGAGCCTCTT GGTTCAAGTG
     GTCTCCGAGA CGGACCGTGG GGAGAGGTCC ACCCCGGAAC AGGGGGTCCC GAGTAGACTC CGTCGAGTCG AATGACCAAT TCTCGGAGAA CCAAGTTCAC

1301 ACCTTGGGCT GCTAATGAAC CTCGGTGCCT CTTGTCCCCA TGTGTAAACA GGGGAAATAA TAGTGCTGTG TCCTAAGGGT TATTGTTTGG ATCAGTGAAG
     TGGAACCCGA CGATTACTTG GAGCCACGGA GAACAGGGGT ACACATTTGT CCCCTTTATT ATCACGACAC AGGATTCCCA ATAACAAACC TAGTCACTTC

1401 TAACTCAAGT TGAATGCTTA GAACAGCCCA TCATACGTAC ATGGTACCCA ATAAATGCTA GCCACTGTGT TATGACTGCC CCACCTCTGC ACCCCAAGTT
     ATTGAGTTCA ACTTACGAAT CTTGTCGGGT AGTATGCATG TACCATGGGT TATTTACGAT CGGTGACACA ATACTGACGG GGTGGAGACG TGGGGTTCAA

1501 CCTGAGCCTC CCCTTCACTC CACTTTGACA CGGCCCCTCC CTTGTGACCT GAGGGCAGGT CCCCACTCTG TCCTGGCAGG AGCGCATGGG CGAGTGTCTG
     GGACTCGGAG GGGAAGTGAG GTGAAACTGT GCCGGGGAGG GAACACTGGA CTCCCGTCCA GGGGTGAGAC AGGACCGTCC TCGCGTACCC GCTCACAGAC

1601 CAGCGCACGG GCACCAGTGT TGTACTCACA TCCATCAACA ACATGGCCGC CTTCCTCATG GCTGCCCTCG TTCCCATCCC TGCGCTGCGA GCCTTCTCCC
     GTCGCGTGCC CGTGGTCACA ACATGAGTGT AGGTAGTTGT TGTACCGGCG GAAGGAGTAC CGACGGGAGC AAGGGTAGGG ACGCGACGCT CGGAAGAGGG

1701 TACAGCCTGG ACCTACGGCG GCGCCACTGC CAGCGCCTTG ATGTGCTCTG CTGCTTCTCC AGGTACTGCC TGCGCCCCAG CCCCTTCCTC CCGTGACCCA
     ATGTCGGACC TGGATGCCGC CGCGGTGACG GTCGCGGAAC TACACGAGAC GACGAAGAGG TCCATGACGG ACGCGGGGTC GGGGAAGGAG GGCACTGGGT

1801 CGCCAGCCTG TCCCCTCACC AGCATTTCAA GGCACAGACC TGTCATCCAC TCTCTACCTC TTCCAGTCCC TGCTCTGCTC AGGTGATTCA GATCCTGCCC
     GCGGTCGGAC AGGGGAGTGG TCGTAAAGTT CCGTGTCTGG ACAGTAGGTG AGAGATGGAG AAGGTCAGGG ACGAGACGAG TCCACTAAGT CTAGGACGGG

1901 CAGGAGCTGG GGGACGGGAC AGTACCAGTG GGCATTGCCC ACCTCACTGC CACAGTTCAA GCCTTTACCC ACTGTGAAGC CAGCAGCCAG CATGTGGTCA
     GTCCTCGACC CCCTGCCCTG TCATGGTCAC CCGTAACGGG TGGAGTGACG GTGTCAAGTT CGGAAATGGG TGACACTTCG GTCGTCGGTC GTACACCAGT

2001 CCATCCTGCC TCCCCAAGCC CACCTGGTGC CCCCACCTTC TGACCCACTG GGCTCTGAGC TCTTCAGCCC TGGAGGGTCC ACACGGGACC TTCTAGGCCA
     GGTAGGACGG AGGGGTTCGG GTGGACCACG GGGGTGGAAG ACTGGGTGAC CCGAGACTCG AGAAGTCGGG ACCTCCCAGG TGTGCCCTGG AAGATCCGGT
```

FIG. 10B

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2101 GGAGGAGGAG ACAAGGCAGA AGGCAGCCTG CAAGTCCCTG CCCTGTGCCC GCTGGAATCT TGCCCATTTC GCCCGCTATC AGTTTGCCCC GTTGCTGCTC
     CCTCCTCCTC TGTTCCGTCT TCCGTCGGAC GTTCAGGGAC GGGACACGGG CGACCTTAGA ACGGGTAAAG CGGGCGATAG TCAAACGGGG CAACGACGAG

2201 CAGTCACATG CCAAGGCCAT CGTGCTGGTG CTCTTTGGTG CTCTTCTGGG CCTGAGCCTC TACGGAGCCA CCTTGGTGCA AGACGGCCTG GCCCTGACGG
     GTCAGTGTAC GGTTCCGGTA GCACGACCAC GAGAAACCAC GAGAAGACCC GGACTCGGAG ATGCCTCGGT GGAACCACGT TCTGCCGGAC CGGGACTGCC

2301 ATGTGGTGCC TCGGGGCACC AAGGAGCATG CCTTCCTGAG CGCCCAGCTC AGGTACTTCT CCCTGTACGA GGTGGCCCTG GTGACCCAGG GTGGCTTTGA
     TACACCACGG AGCCCCGTGG TTCCTCGTAC GGAAGGACTC GCGGGTCGAG TCCATGAAGA GGGACATGCT CCACCGGGAC CACTGGGTCC CACCGAAACT

2401 CTACGCCCAC TCCCAACGCG CCCTCTTTGA TCTGCACCAG CGCTTCAGTT CCCTCAAGGC GGTGCTGCCC CCACCGGCCA CCCAGGCACC CCGCACCTGG
     GATGCGGGTG AGGGTTGCGC GGGAGAAACT AGACGTGGTC GCGAAGTCAA GGGAGTTCCG CCACGACGGG GGTGGCCGGT GGGTCCGTGG GGCGTGGACC

2501 CTGCACTATT ACCGCAACTG GCTACAGGGA ATCCAGGCTG CCTTTGACCA GGACTGGGCT TCTGGGCGCA TCACCCGCCA CTCGTACCGC AATGGCTCTG
     GACGTGATAA TGGCGTTGAC CGATGTCCCT TAGGTCCGAC GGAAACTGGT CCTGACCCGA AGACCCGCGT AGTGGGCGGT GAGCATGGCG TTACCGAGAC

2601 AGGATGGGGC CCTGGCCTAC AAGCTGCTCA TCCAGACTGG AGACGCCCAG GAGCCTCTGG ATTTCAGCCA GGTTGGGAGA GGGCTGGAGG GGTCCACTAG
     TCCTACCCCG GGACCGGATG TTCGACGAGT AGGTCTGACC TCTGCGGGTC CTCGGAGACC TAAAGTCGGT CCAACCCTCT CCCGACCTCC CCAGGTGATC

2701 TACAGGGGCT GCAGGCCTCC TGGGCCCAGG CCTTCAGCCC TCTCTGCCTC TGCAGCTGAC CACAAGGAAG CTGGTGGACA GAGAGGGACT GATTCCACCC
     ATGTCCCCGA CGTCCGGAGG ACCCGGGTCC GGAAGTCGGG AGAGACGGAG ACGTCGACTG GTGTTCCTTC GACCACCTGT CTCTCCCTGA CTAAGGTGGG

2801 GAGCTCTTCT ACATGGGGCT GACCGTGTGG GTGAGCAGTG ACCCCCTGGG TCTGGCAGCC TCACAGGCCA ACTTCTACCC CCCACCTCCT GAATGGCTGC
     CTCGAGAAGA TGTACCCCGA CTGGCACACC CACTCGTCAC TGGGGGACCC AGACCGTCGG AGTGTCCGGT TGAAGATGGG GGGTGGAGGA CTTACCGACG

2901 ACGACAAATA CGACACCACG GGGGAGAACC TTCGCAGTGA GTCTTGGGGG GAGCTCGGCA AGAGCCTCAG CCTCGCCCAC ACAAGCCCTG AGCCTGAGGC
     TGCTGTTTAT GCTGTGGTGC CCCCTCTTGG AAGCGTCACT CAGAACCCCC CTCGAGCCGT TCTCGGAGTC GGAGCGGGTG TGTTCGGGAC TCGGACTCCG

3001 CCTGCCCACT CTGCCCCGTG CTCACCGCCC TGTCCCTCTC CCTCTTCTCC CTTCCCCTCC CCTCCACAGT CCCGCCAGCT CAGCCCTTGG AGTTTGCCCA
     GGACGGGTGA GACGGGGCAC GAGTGGCGGG ACAGGGAGAG GGAGAAGAGG GAAGGGGAGG GGAGGTGTCA GGGCGGTCGA GTCGGGAACC TCAAACGGGT
```

FIG. 10C

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3101 GTTCCCCTTC CTGCTGCGTG GCCTCCAGAA GACTGCAGAC TTTGTGGAGG CCATCGAGGG GGCCCGGGCA GCATGCGCAG AGGCCGGCCA GGCTGGGGTG
     CAAGGGGAAG GACGACGCAC CGGAGGTCTT CTGACGTCTG AAACACCTCC GGTAGCTCCC CCGGGCCCGT CGTACGCGTC TCCGGCCGGT CCGACCCCAC

3201 CACGCCTACC CCAGCGGCTC CCCCTTCCTC TTCTGGGAAC AGTATCTGGG CCTGCGGCGC TGCTTCCTGC TGGCCGTCTG CATCCTGCTG GTGTGCACTT
     GTGCGGATGG GGTCGCCGAG GGGGAAGGAG AAGACCCTTG TCATAGACCC GGACGCCGCG ACGAAGGACG ACCGGCAGAC GTAGGACGAC CACACGTGAA

3301 TCCTCGTCTG TGCTCTGCTG CTCCTCAACC CCTGGACGGC TGGCCTCATA GTGAGTGCTT GCAGGAGTGG GGACAGAGAC ACCCCACCCT TCCCTGCCCA
     AGGAGCAGAC ACGAGACGAC GAGGAGTTGG GGACCTGCCG ACCGGAGTAT CACTCACGAA CGTCCTCACC CCTGTCTCTG TGGGGTGGGA AGGGACGGGT

3401 GCCTGTCATC CCTCCTGCCA GGAGCCCTCT GTGAGCCCTG TCTCCCTCAG GTGCTGGTCC TGGCGATGAT GACAGTGGAA CTCTTTGGTA TCATGGGTTT
     CGGACAGTAG GGAGGACGGT CCTCGGGAGA CACTCGGGAC AGAGGGAGTC CACGACCAGG ACCGCTACTA CTGTCACCTT GAGAAACCAT AGTACCCAAA

3501 CCTGGGCATC AAGCTGAGTG CCATCCCCGT GGTGATCCTT GTGGCCTCTG TAGGCATTGG CGTTGAGTTC ACAGTCCACG TGGCTCTGGT GAGCACGGGC
     GGACCCGTAG TTCGACTCAC GGTAGGGGCA CCACTAGGAA CACCGGAGAC ATCCGTAACC GCAACTCAAG TGTCAGGTGC ACCGAGACCA CTCGTGCCCG

3601 ACCCCGGGGA GGGACCAATC AGCTGATTCA GTATTCAACA CATATTGTTC AAGCCCCTAC TATGTGCTAG GTACTATTTA AGAATTTGGG CTGGGTGGAC
     TGGGGCCCCT CCCTGGTTAG TCGACTAAGT CATAAGTTGT GTATAACAAG TTCGGGGATG ATACACGATC CATGATAAAT TCTTAAACCC GACCCACCTG

3701 GTGGTGGCTC ATTCCTGTAA TCCCAGCACT TTGGGAGGCC GAGGCGGGTG GATCACCTGA GGTCGGGAGT TCGAAACCAG CCTGGCCAAC ATGGTGAAAC
     CACCACCGAG TAAGGACATT AGGGTCGTGA AACCCTCCGG CTCCGCCCAC CTAGTGGACT CCAGCCCTCA AGCTTTGGTC GGACCGGTTG TACCACTTTG

3801 CCTGTCTTTA CTAAAAATAC AAAAAATTAG CCAGGCGTGG TGGCACATGC CAGTAGTCCC AGCTACTTTG GAGGCTGAGG CAGAATTGCT TGAACCTGGG
     GGACAGAAAT GATTTTTATG TTTTTTAATC GGTCCGCACC ACCGTGTACG GTCATCAGGG TCGATGAAAC CTCCGACTCC GTCTTAACGA ACTTGGACCC

3901 AGGCGAAGGT TGCAGTGAGC TGAGATCGTG CCATTGCACT CCAGCCTGGG CAACAAGAGT GCAACTCTCC GTCTCAAAAA AAAAAAAAAA AAGGGCGGCC
     TCCGCTTCCA ACGTCACTCG ACTCTAGCAC GGTAACGTGA GGTCGGACCC GTTGTTCTCA CGTTGAGAGG CAGAGTTTTT TTTTTTTTTT TTCCCGCCGG

4001 GCGA
     CGCT
```

FIG. 10D

~~Clone 16.1 human patched 2~~
~~length: 2002 bp~~

~~(SEQ ID NO:9)~~

```
   1 TTCCGGCATG ACTCGATCGC CGCCCCTCAG AGAGCTGCCC CCGAGTTACA CACCCCCAGC TCGAACCGCA GCACCCCAGA TCCTAGCTGG GAGCCTGAAG
     AAGGCCGTAC TGAGCTAGCG GCGGGGAGTC TCTCGACGGG GGCTCAATGT GTGGGGGTCG AGCTTGGCGT CGTGGGGTCT AGGATCGACC CTCGGACTTC

 101 GCTCCACTCT GGCTTCGTGC TTACTTCCAG GGCCTGCTCT TCTCTCTGGG ATGCGGGATC CAGAGACATT GTGGCAAAGT GCTCTTTCTG GGACTGTTGG
     CGAGGTGAGA CCGAAGCACG AATGAAGGTC CCGGACGAGA AGAGAGACCC TACGCCCTAG GTCTCTGTAA CACCGTTTCA CGAGAAAGAC CCTGACAACC

 201 CCTTTGGGGC CCTGGCATTA GGTCTCCGCA TGGCCATTAT TGAGACAAAC TTGGAACAGC TCTGGGTAGA AGTGGGCAGC CGGGTGAGCC AGGAGCTGCA
     GGAAACCCCG GGACCGTAAT CCAGAGGCGT ACCGGTAATA ACTCTGTTTG AACCTTGTCG AGACCCATCT TCACCCGTCG GCCCACTCGG TCCTCGACGT

 301 TTACACCAAG GAGAAGCTGG GGGAGGAGGC TGCATACACC TCTCAGATGC TGATACAGAC CGCACGCCAG GAGGGAGAGA ACATCCTCAC ACCCGAAGCA
     AATGTGGTTC CTCTTCGACC CCCTCCTCCG ACGTATGTGG AGAGTCTACG ACTATGTCTG GCGTGCGGTC CTCCCTCTCT TGTAGGAGTG TGGGCTTCGT

 401 CTTGGCCTCC ACCTCCAGGC AGCCCTCACT GCCAGTAAAG TCCAAGTATC ACTCTATGGG AAGTCCTGGG ATTTGAACAA AATCTGCTAC AAGTCAGGAG
     GAACCGGAGG TGGAGGTCCG TCGGGAGTGA CGGTCATTTC AGGTTCATAG TGAGATACCC TTCAGGACCC TAAACTTGTT TTAGACGATG TTCAGTCCTC

 501 TTCCCCTTAT TGAAAATGGA ATGATTGAGT GGATGATTGA GAAGCTGTTT CCGTGCGTGA TCCTCACCCC CCTGGACTGC TTCTGGGAGG GAGCCAAACT
     AAGGGGAATA ACTTTTACCT TACTAACTCA CCTACTAACT CTTCGACAAA GGCACGCACT AGGAGTGGGG GGAGCTGACG AAGACCCTCC CTCGGTTTGA

 601 CCAAGGGGGC TCCGCCTACC TGCCCGGCCG CCCGGATATC CAGTGGACCA ACCTGGATCC AGAGCAGCTG CTGGAGGAGC TGGGTCCCTT TGCCTCCCTT
     GGTTCCCCCG AGGCGGATGG ACGGGCCGGC GGGCCTATAG GTCACCTGGT TGGACCTAGG TCTCGTCGAC GACCTCCTCG ACCCAGGGAA ACGGAGGGAA

 701 GAGGGCTTCC GGGAGCTGCT AGACAAGGCA CAGGTGGGCC AGGCCTACGT GGGGCGGCCC TGTCTGCACC CTGATGACCT CCACTGCCCA CCTAGTGCCC
     CTCCCGAAGG CCCTCGACGA TCTGTTCCGT GTCCACCCGG TCCGGATGCA CCCCGCCGGG ACAGACGTGG GACTACTGGA GGTGACGGGT GGATCACGGG

 801 CCAACCATCA CAGCAGGCAG GCTCCCAATG TGGCTCACGA GCTGAGTGGG GGCTGCCATG GCTTCTCCCA CAAATTCATG CACTGGCAGG AGGAATTGCT
     GGTTGGTAGT GTCGTCCGTC CGAGGGTTAC ACCGAGTGCT CGACTCACCC CCGACGGTAC CGAAGAGGGT GTTTAAGTAC GTGACCGTCC TCCTTAACGA

 901 GCTGGGAGGC ATGGCCAGAG ACCCCCAAGG AGAGCTGCTG AGGGCAGAGG CCCTGCAGAG CACCTTCTTG CTGATGAGTC CCCGCCAGCT GTACGAGCAT
     CGACCCTCCG TACCGGTCTC TGGGGGTTCC TCTCGACGAC TCCCGTCTCC GGGACGTCTC GTGGAAGAAC GACTACTCAG GGGCGGTCGA CATGCTCGTA
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FIG. 11A

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1001 TTCCGGGGTG ACTATCAGAC ACATGACATT GGCTGGAGTG AGGAGCAGGC CAGCACAGTG CTACAAGCCT GGCAGCGGCG CTTTGTGCAG CTGGCCCAGG
     AAGGCCCCAC TGATAGTCTG TGTACTGTAA CCGACCTCAC TCCTCGTCCG GTCGTGTCAC GATGTTCGGA CCGTCGCCGC GAAACACGTC GACCGGGTCC

1101 AGGCCCTGCC TGAGAACGCT TCCCAGCAGA TCCATGCCTT CTCCTCCACC ACCCTGGATA ACATCCTGCA TGCGTTCTCT GAAGTCAGTG CTGCCCGTGT
     TCCGGGACGG ACTCTTGCGA AGGGTCGTCT AGGTACGGAA GAGGAGGTGG TGGGACCTAT TGTAGGACGT ACGCAAGAGA CTTCAGTCAC GACGGGCACA

1201 GGTGGGAGGC TATCTGCTCA TGCTGGCCTA TGCCTGTGTG ACCATGCTGC GGTGGGACTG CGCCCAGTCC CAGGGTTCCG TGGGCCTTGC CGGGGTACTG
     CCACCCTCCG ATAGACGAGT ACGACCGGAT ACGGACACAC TGGTACGACG CCACCCTGAC GCGGGTCAGG GTCCCAAGGC ACCCGGAACG GCCCCATGAC

1301 CTGGTGGCCC TGGCGGTGGC CTCAGGCCTT GGGCTCTGTG CCCTGCTCGG CATCACCTTC AATGCTGCCA CTACCCAGGT GCTGCCCTTC TTGGCTCTGG
     GACCACCGGG ACCGCCACCG GAGTCCGGAA CCCGAGACAC GGGACGAGCC GTAGTGGAAG TTACGACGGT GATGGGTCCA CGACGGGAAG AACCGAGACC

1401 GAATCGGCGT GGATGACGTA TTCCTGCTGG CGCATGCCTT CACAGAGGCT CTGCCTGGCA CCCCTCTCCA GGAGCGCATG GGCGAGTGTC TGCAGCGCAC
     CTTAGCCGCA CCTACTGCAT AAGGACGACC GCGTACGGAA GTGTCTCCGA GACGGACCGT GGGGAGAGGT CCTCGCGTAC CCGCTCACAG ACGTCGCGTG

1501 GGGCACCAGT GTCGTACTCA CATCCATCAA CAACATGGCC GCCTTCCTCA TGGCTGCCCT CGTTCCCATC CCTGCGCTGC GAGCCTTCTC CTTACAGCCA
     CCCGTGGTCA CAGCATGAGT GTAGGTAGTT GTTGTACCGG CGGAAGGAGT ACCGACGGGA GCAAGGGTAG GGACGCGACG CTCGGAAGAG GAATGTCGGT

1601 TCCTCAGCCT GGACCTACGG CGGCGCCACT GCCAGCGCCT TGATGTGCTC TGCTGCTTCT CCAGTCCCTG CTCTGCTCAG GTGATTCAGA TCCTGCCCCA
     AGGAGTCGGA CCTGGATGCC GCCGCGGTGA CGGTCGCGGA ACTACACGAG ACGACGAAGA GGTCAGGGAC GAGACGAGTC CACTAAGTCT AGGACGGGGT

1701 GGAGCTGGGG GACGGGACAG TACCAGTGGG CATTGCCCAC CTCACTGCCA CAGTTCAAGC CTTTACCCAC TGTGAAGCCA GCAGCCAGCA TGTGGTCACC
     CCTCGACCCC CTGCCCTGTC ATGGTCACCC GTAACGGGTG GAGTGACGGT GTCAAGTTCG GAAATGGGTG ACACTTCGGT CGTCGGTCGT ACACCAGTGG

1801 ATCCTGCCTC CCCAAGCCCA CCTGGTGCCC CCACCTTCTG ACCCACTGGG CTCTGAGCTC TTCAGCCCTG GAGGGTCCAC ACGGGACCTT CTAGGCCAGG
     TAGGACGGAG GGGTTCGGGT GGACCACGGG GGTGGAAGAC TGGGTGACCC GAGACTCGAG AAGTCGGGAC CTCCCAGGTG TGCCCTGGAA GATCCGGTCC

1901 AGGAGGAGAC AAGGCAGAAG GCAGCCTGCA AGTCCCTGCC CTGTGCCCGC TGGAATCTTG CCCATTTCGC CCCGGAATTC CTGCAGCCCG GGGGATCCAC
     TCCTCCTCTG TTCCGTCTTC CGTCGGACGT TCAGGGACGG GACACGGGCG ACCTTAGAAC GGGTAAAGCG GGGCCTTAAG GACGTCGGGC CCCCTAGGTG

2001 TAGTTCTAGA GCGGCCGCCA CCGCGGTGGA GCTCCAGCTT TTGTTCCCTT TAGTGAGGGT TAATTGCGCG CTTGGGTATC TT
     ATCAAGATCT CGCCGGCGGT GGCGCCACCT CGAGGTCGAA AACAAGGGAA ATCACTCCCA ATTAACGCGC GAACCCATAG AA
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FIG. 11B

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